VOLUME 52 NUMBER 1 JULY, 1961

AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

CONTENTS

For a complete table of contents see page xxxix

Publication office: Curtis Reed Plaza, Menasha, Wisconsin

Subscription price in United States twelve dollars yearly. In Canada and foreign countries fourteen dollars. Published monthly by the Ophthalmic Publishing Company. Subscription and Advertising Office: 664 North Michigan Avenue, Chicago 11, Illinois. Second class postage has been paid at the post office at Menasha, Wisconsin. Printed in U S.A.

A 'COMPLETE' MIOTIC

The present treatment of chronic simple glaucoma is generally conceded to be a long-term "holding" operation—prevention of disease progression. Effective therapy is not just . . . "immediate control of elevated intra-ocular pressure", but also, assurance that control *will be routinely maintained* for a period of many years by the patient. To accomplish this aim PILOFRIN presents several important advantages—to physician and patient . . .

- In FORMULA—Pilocarpine nitrate (in 6 different strengths) for proven, uncomplicated pressure control. Phenylephrine HCl (0.12%) for prompt and reliable decongestion. Methylcellulose (0.5%) for lubrication and prolongation of the miotic's action.
- In ESTHETICS—The decongestant and lubricant help offset the irritation, redness and other subjective complaints so common with the miotics—promotes continuous patient cooperation.
- In FLEXIBILITY—Six strengths of pilocarpine . . . ½%, 1%, 2%, 3%, 4%, 6% . . . for suitably-tailored control of each patient. Available in 15 cc. bottles.

Pilofrin™
Ophthalmic Solution . . . for glaucoma

ALLERGAN PHARMACEUTICALS Los Angeles 17, Calif.

acute conjunctivitis before treatment

clinical photographs

truly soluble—for fast relief of inflammation

0.1% OPHTHALMIC SOLUTION

NeoDecadron®

DEXAMETHASONE 21-PHOSPHATE—NEOMYCIN SULFATE

INDICATIONS: Trauma—mechanical, chemical or thermal; inflammation of the conjunctiva, cornea, or uveal tract involving the anterior segment; allergy; blepharitis.

CAUTION: Steroid therapy should never be employed in the presence of tuberculosis or herpes simplex.

NeoDECADRON is also available as the ophthalmic ointment (.05%). Ointment and solution are available with dexamethasone 21-phosphate alone: DECADRON® Phosphate Ophthalmic Solution and DECADRON Phosphate Ophthalmic Ointment.

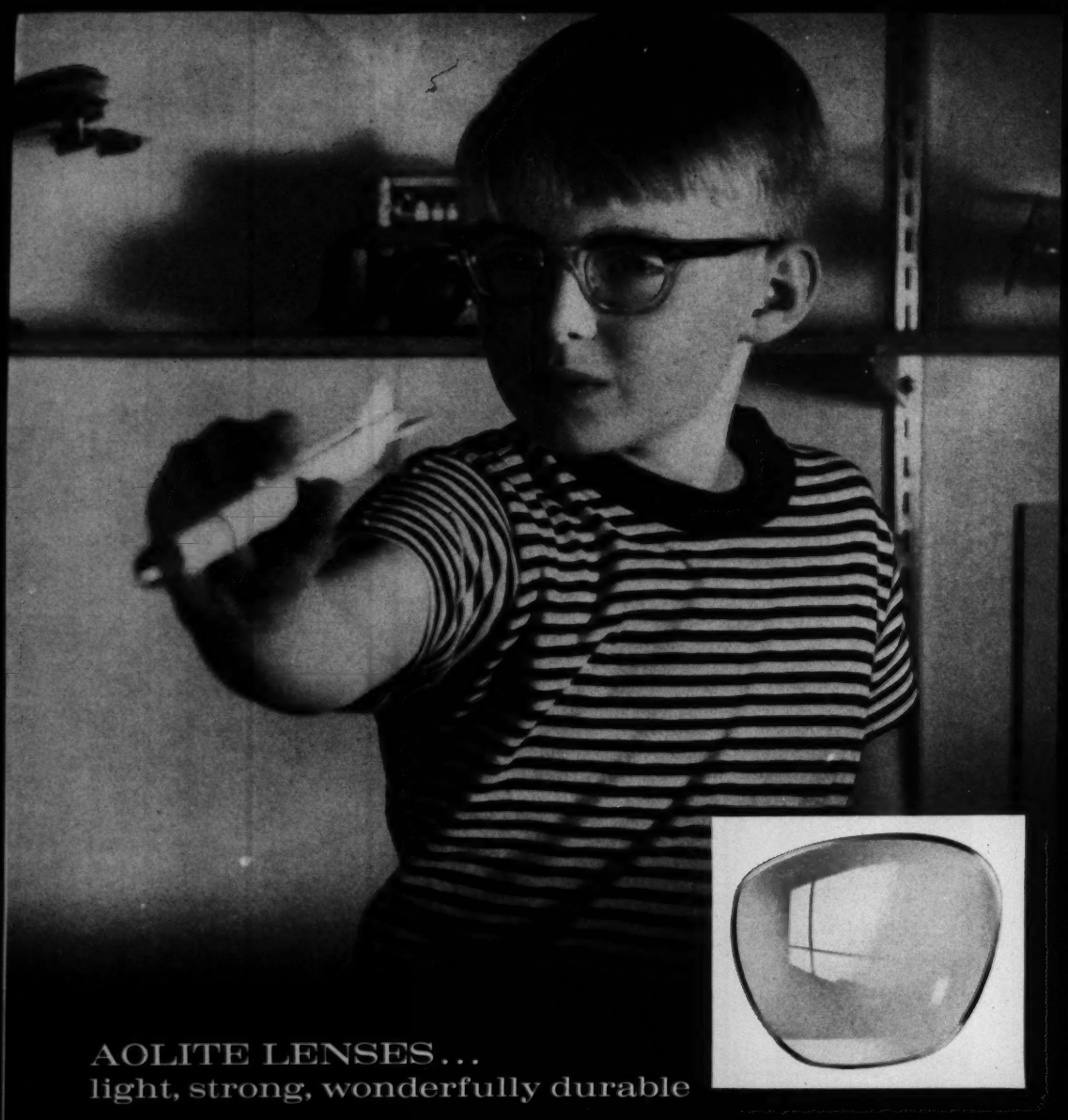
• unexcelled steroid activity • in true solution for peak effectiveness . . . maximal contact at the site of the lesion • superior patient comfort—no irritating particles • quick-acting, broad antimicrobial activity.

Additional information is available to physicians on request.
NeoDECADRON and DECADRON are trademarks of Merck & Co., INC.

MSD

MERCK SHARP & DOHME
Division of Merck & Co., INC., West Point, Pa.

4 days after treatment



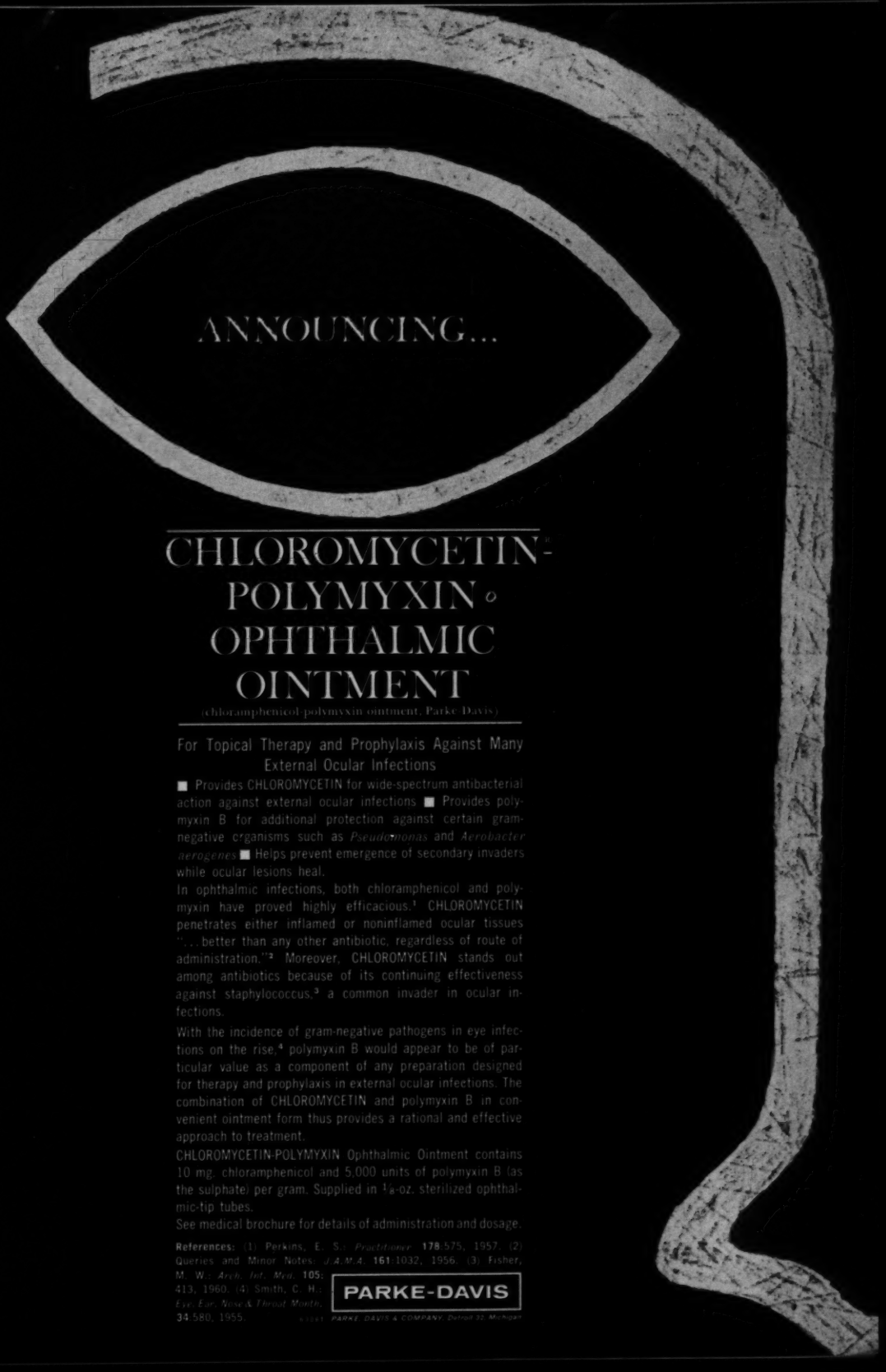
AOLITE LENSES...
light, strong, wonderfully durable

For active people of all ages—and particularly school children—prescribe new AOLITE lenses. These lenses are twice as light as glass, 23 times more impact-resistant; they're 20 to 40 times more scratch-resistant than ordinary plastic lenses. These truly comfortable lenses also filter out ultraviolet rays, resist "fogging," and replacement is guaranteed if accidentally broken. Moreover, AOLITE lenses come to you in a complete range of foci and in either white or Uniform Density Green, Tan, Pink or Grey. So for the best-in-sight for back-to-school, specify AOLITE, available through your local AO Branch or AO Franchised Distributor.

American Optical
COMPANY

Since 1833... Better Vision for Better Living

A participating sponsor
of the OMA-BVI
Industry Promotion Program.



CHLOROMYCETIN®-POLYMYXIN B OPHTHALMIC OINTMENT

(chloramphenicol-polymyxin ointment, Parke-Davis)

For Topical Therapy and Prophylaxis Against Many External Ocular Infections

■ Provides CHLOROMYCETIN for wide-spectrum antibacterial action against external ocular infections. ■ Provides polymyxin B for additional protection against certain gram-negative organisms such as *Pseudomonas* and *Aerobacter aerogenes*. ■ Helps prevent emergence of secondary invaders while ocular lesions heal.

In ophthalmic infections, both chloramphenicol and polymyxin have proved highly efficacious.[1] CHLOROMYCETIN penetrates either inflamed or noninflamed ocular tissues "...better than any other antibiotic, regardless of route of administration."[2] Moreover, CHLOROMYCETIN stands out among antibiotics because of its continuing effectiveness against staphylococcus,[3] a common invader in ocular infections.

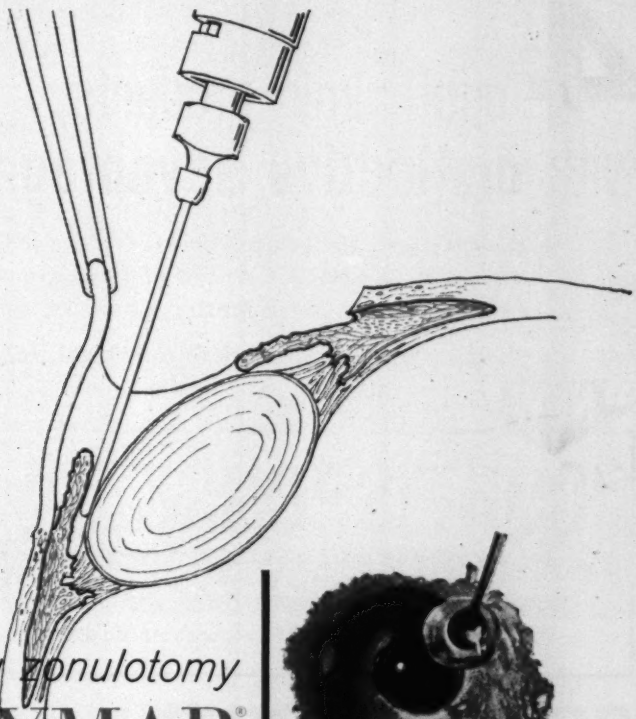
With the incidence of gram-negative pathogens in eye infections on the rise,[4] polymyxin B would appear to be of particular value as a component of any preparation designed for therapy and prophylaxis in external ocular infections. The combination of CHLOROMYCETIN and polymyxin B in convenient ointment form thus provides a rational and effective approach to treatment.

CHLOROMYCETIN-POLYMYXIN Ophthalmic Ointment contains 10 mg. chloramphenicol and 5,000 units of polymyxin B (as the sulphate) per gram. Supplied in $\frac{1}{8}$-oz. sterilized ophthalmic-tip tubes.

See medical brochure for details of administration and dosage.

References: (1) Perkins, E. S.: *Practitioner* **178**:575, 1957. (2) Queries and Minor Notes: *J.A.M.A.* **161**:1032, 1956. (3) Fisher, M. W.: *Arch. Int. Med.* **105**:413, 1960. (4) Smith, C. H.: *Eye, Ear, Nose & Throat Month.* **34**:580, 1955.

PARKE-DAVIS



fast replacing zonulotomy

Alpha CHYMAR®

ALPHA CHYMOTRYPSIN

Alpha Chymar offers an outstanding advance in technique over mechanical zonulysis. Many thousands of lens removals have been made easier through use of this agent, which dissolves or greatly weakens the zonular fibers so that the lens may be slipped out.[1-4] This simplified manipulation helps to avoid the incidence of capsular rupture and zonular traction on structures of the inner eye, often encountered during mechanical removal.[5]

Commenting on the ease of the technique, one operator has remarked that "alpha chymotrypsin still is far superior to any other technic I have ever used or have observed."[2]

1. Cogan, J. E. H.: Proc. Roy. Soc. Med. *51*:927, 1958. 2. Jenkins, B. H.: South. M. J. *53*:44, 1960; discussion by Raiford, M. B. 3. Raiford, M. B.: J.M.A. Georgia *48*:163, 1959. 4. Rizzuti, A. B.: A.M.A. Arch. Ophth. *61*:135, 1959. 5. Thorpe, H. E.: Am. J. Ophth. *49*:531, 1960.

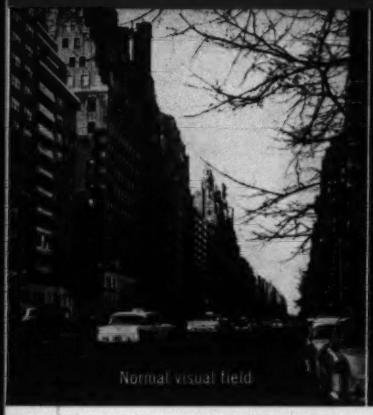
ARMOUR PHARMACEUTICAL COMPANY
KANKAKEE, ILLINOIS
Armour Means Protection

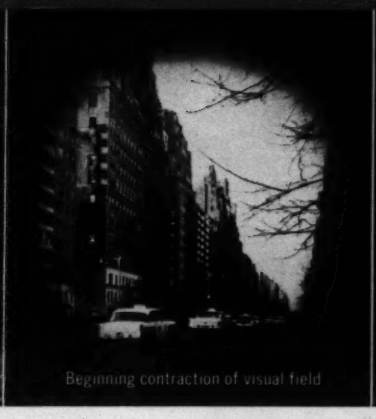
***Alpha* CHYMAR**

For Ophthalmic Use

Alpha Chymar is a lyophilized form of crystallized alpha chymotrypsin, a proteolytic enzyme obtained from mammalian pancreas. The contents of the vial when reconstituted with 5 cc. of Alpha Chymar Diluent provide a solution containing 150 Armour Units per cc.—comparable to a 1-5000 dilution. ACTION AND USES: Alpha Chymar is specific for lysis of the zonule in lens extraction. The lytic action is a selective one that does not adversely affect the hyaloid membrane, lens capsule, or other intra-ocular structures. ADMINISTRATION: Used intra-ocularly. For suggested procedure in cataract surgery see package insert. CONTRAINDICATIONS: Until additional reports are obtained, the use of Alpha Chymar is not advised in children under ten years of age. SUPPLIED: Cartons of 5 packages—each package contains one vial of lyophilized Alpha Chymar and one vial of Alpha Chymar Diluent (Sodium Chloride Injection, U.S.P.). For special precautions regarding reconstitution and handling, see package insert.

for topical therapy
of certain types of
GLAUCOMA...


Normal visual field


Beginning contraction of visual field


Advanced contraction of visual field

...two highly effective miotics

HUMORSOL®

Demecarium Bromide

•potent, longer-acting than other miotics •two instillations weekly are often sufficient to control glaucoma •because it is unusually potent, it may be uniquely useful in breaking up peripheral synechiae •aqueous—isotonic with conjunctival fluid •stable—refrigeration not required •0.25% ophthalmic solution, in 5-cc. bottle with dropper

FLOROPRYL®

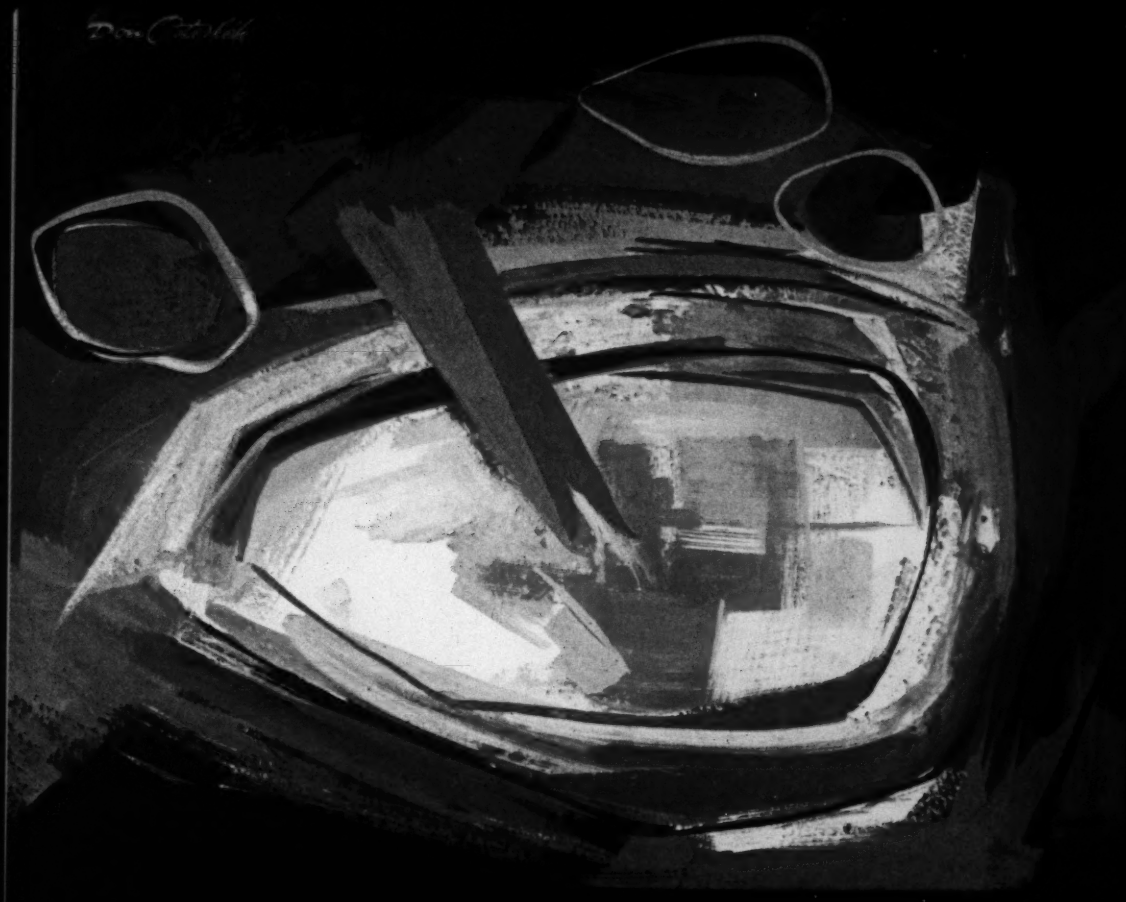
Isoflurophate U.S.P.

•long-acting—in glaucoma, one instillation daily is often sufficient; (in strabismus, one instillation every two days to one week) •may be effective when other agents fail •two topical dosage forms—0.1% ophthalmic solution in anhydrous peanut oil, in 5-cc. bottle with dropper; 0.025% ophthalmic ointment, in 3.5 Gm. tubes

also available: DARANIDE® Dichlorphenamide **for oral control of intraocular pressure, 50-mg. tablets**

Before prescribing or administering HUMORSOL, FLOROPRYL and DARANIDE, the physician should consult the detailed information on use accompanying the package or available on request.

MSD MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., WEST POINT, PA.



for open-angle glaucoma

EPPY: A NEW *l*-EPINEPHRINE COMPLEX

that does not sting . . .
and needs no refrigeration

EPPY is *l*-epinephrine U.S.P. 1% in a sterile buffered isotonic vehicle preserved with sodium bisulfite 0.3% and oxine sulfate 0.01%.

Buffered to the physiological pH of 7.4, **EPPY** is compatible with tears and causes no stinging.

Containing the *l*-epinephrine in a stabilized free-base complex form (not a salt), **EPPY** needs no refrigeration during storage or normal use by patients.

EPPY is supplied in a 7.5 cc bottle with separate sterile dropper assembly.

For your sample and complete literature, write to
Barnes-Hind Ophthalmic Products, Inc.
895 Kifer Road, Sunnyvale, Calif.

when allergens bring tears

Optihist®

relieves itching, burning, redness and edema

It's hay fever time! Soft breezes blow allergens everywhere. And well your patients know it, for their eyes are itching, burning, and tearing—to their great discomfort.

Optihist brings prompt relief; combines useful antihistaminic and decongestant properties with mild analgesic action. Edema, tearing and redness are dispelled. Itching and burning are relieved without interference with the corneal reflex. Only two drops every few hours provide welcome relief.

Optihist contains chlorpheniramine maleate 0.3%, phenylephrine HCl 0.08%, piperocaine HCl 0.5%, methylcellulose 0.33%, in isotonic buffered solution of boric acid, potassium chloride and sodium carbonate preserved with benzalkonium chloride 0.01% and disodium ethylenediamine tetracetate 0.01%.

Warning: Use cautiously in patients with diabetes, hypertension, or glaucoma, and in the aged.

Caution: Federal law prohibits dispensing without a prescription.

Supplied in 15 cc. sterile Lacrivials.®

ISO-SOL® sterile ophthalmic preparations

CROOKES-BARNES Laboratories, Inc.
Wayne, New Jersey

IN EYE INFECTIONS

broad antibacterial range

effective anti-inflammatory action

OPHTHOCORT

chloramphenicol-polymyxin B-hydrocortisone ointment, Parke-Davis

OPHTHOCORT provides:

Chloromycetin® (chloramphenicol, Parke-Davis) for prompt, wide-spectrum antibacterial action[1-6]

Polymyxin B for additional control of gram-negative invaders, including *Pseudomonas aeruginosa* [1,7]

Hydrocortisone to decrease inflammation, reduce discomfort, and to lessen danger of tissue scarring[8]

OPHTHOCORT affords: wide-spectrum antibacterial, anti-inflammatory, and antiallergic action in ocular inflammation complicated by infection.

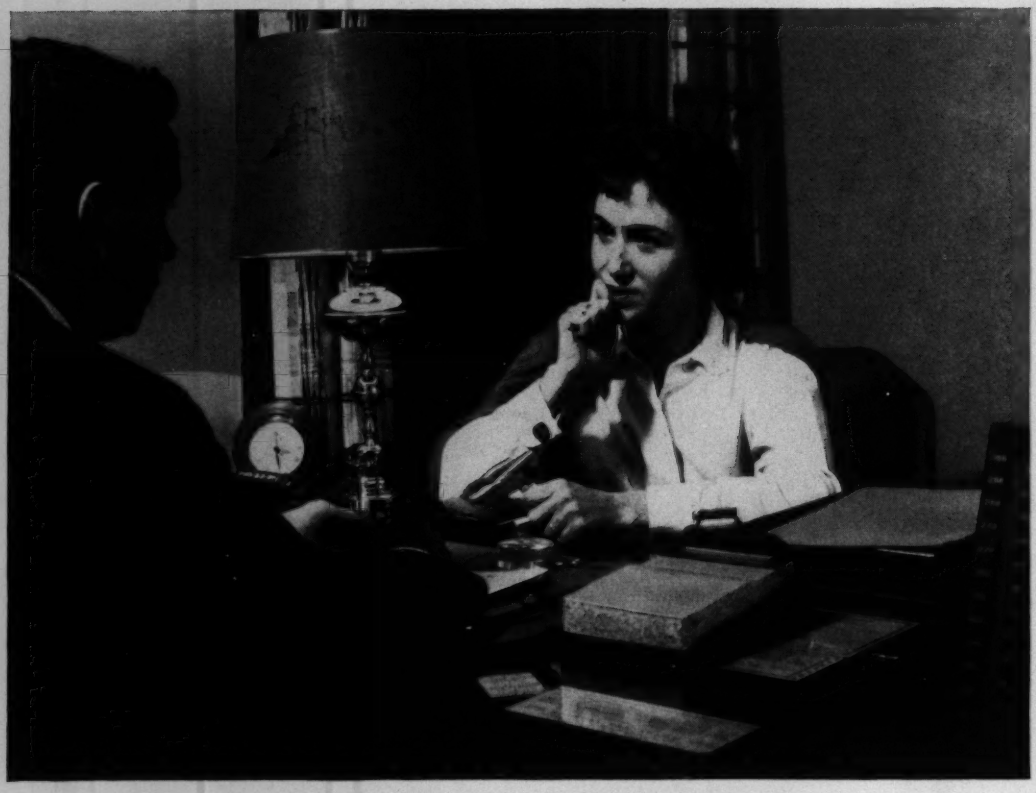
Each gram of Ophthocort contains 10 mg. chloramphenicol, 5 mg. hydrocortisone acetate, 5,000 units polymyxin B sulfate in a special base of liquid petrolatum and polyethylene. *Supplied* in ⅛-oz tubes. *Precautions:* Contraindicated in herpetic infections and ocular tuberculosis. When hydrocortisone is applied locally in treating bacterial diseases of the eye, care must be exercised to assure that the condition is not actually progressing while the external appearance improves. *See medical brochure for details of administration and dosage.*

References: (1) Morrison, W. H.: *Nebraska M. J.* 45:106, 1960. (2) Perkins, E. S.: *Practitioner* 178:575, 1957. (3) Tassman, W. S.: *U. S. Armed Forces M. J.* 10:161, 1959. (4) Kamiya, S.: *Am. J. Ophth.* 42:269, 1956. (5) Holland, R. W. B.: *Arch. Ophth.* 57:214, 1957. (6) Benton, C. D., Jr.: *South M. J.* 51:1562, 1958. (7) Blakiston's New Gould Medical Dictionary, ed. 2, New York, McGraw-Hill Book Company, Inc., 1956, p. 945. (8) Ostler, H. B., & Braley, A. E.: *J. Iowa M. Soc.* 44:427, 1954.

53041

PARKE-DAVIS

PARKE, DAVIS & COMPANY, Detroit 32, Michigan



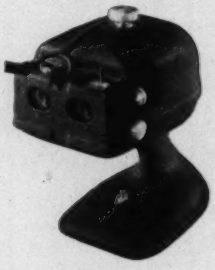
ANISEIKONIA?

The results of a long term survey (15 years) show that at least one out of every ten patients had symptoms that indicated the desirability of an examination for aniseikonia.

Now, whenever case histories or symptoms show possible presence of this disturbing factor, you can make the necessary tests in your own office...quickly, easily and accurately...with the AO Space Eikonometer.

An ingenious lens system and target design reduce examination time to minutes instead of hours. Simple, critically accurate subjective testing is provided for image size differences in horizontal, vertical and oblique meridians. Only 6¾″ x 9¼″ of table space is required.

It will pay you to talk to your Sales Representative about the advantages of "on-the-spot" aniseikonia examinations...a very real way in which you can give added service to many more of your patients.



NOW Many practitioners are using simplified translation tables to design and procure aniseikonic lenses locally at a radical reduction in time and cost.

American Optical COMPANY

INSTRUMENT DIVISION, BUFFALO 15, NEW YORK

Dept. U253

Please send complete information on the AO Space Eikonometer.

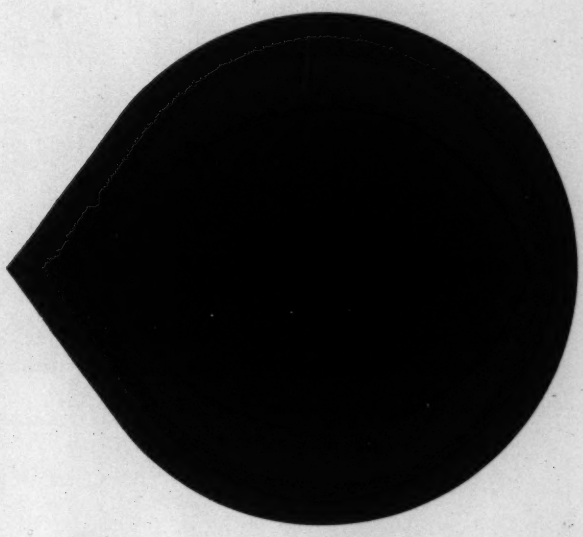
Name_____

Address_____

City_____ Zone____ State_____

OMA BVI

A participating sponsor in the OMA-BVI Industry Promotion Program



YOU CAN SAVE SIGHT WITH UREVERT®

30% urea—lyophilized and specially processed in TRAVERT® (invert sugar solution 10% in water)

REDUCES INTRAOCULAR PRESSURE EVEN IF MIOTICS AND CARBONIC ANHYDRASE INHIBITORS HAVE FAILED

IN ACUTE ANGLE CLOSURE GLAUCOMA—
"dramatic response."

IN PREPARATION FOR INTRAOCULAR SURGERY—
"effective in cases in which carbonic anhydrase inhibitors had little or no effect."

IN RETINAL DETACHMENT SURGERY—
In 15 of 26 scleral buckling procedures "its use was definitely helpful."

IN ORBITAL SURGERY—
"orbital exploration has definitely been facilitated."

Reference: Javid, M., and Davis, M.: Scientific Exhibit No. 922, A.M.A. Annual Meeting (June) 1960.

UREVERT can relieve intraocular pressure when other agents fail because it works by osmosis and is not dependent on the normal outflow mechanisms of the eye. UREVERT was developed at the University of Wisconsin where more than four years of basic and clinical study have demonstrated its extraordinary efficacy.

For complete information about UREVERT, ask your TRAVENOL representative, or write our Professional Service Department.

Cautions: 1. In older patients, do not use lower extremity infusion. 2. UREVERT may temporarily maintain blood pressure in spite of considerable blood loss.

Contraindications: 1. Severely impaired renal or hepatic function. 2. Active intracranial bleeding. 3. Marked dehydration.

Bibliography: 1. Javid, M.: Surg. Clin. North Am. *38*:907 (Aug.) 1958. 2. Galin, M. A.; Aizawa, F., and McLean, J. M.: Am. J. Ophth. *50*:379, 1960. 3. Tarter, R. C., and Linn, J. G., Jr.: A clinical study of the use of intravenous urea in glaucoma (to be published). 4. Hill, K.; Whitney, J. B., and Trotter, R. R.: A.M.A. Arch. Ophth. *65*:497 (April) 1961. 5. Davis, M. D.; Duehr, P. A., and Javid, M.: A.M.A. Arch. Ophth. *65*:526 (April) 1961.

TRAVENOL LABORATORIES, INC., Morton Grove, Ill.

EYES RIGHT

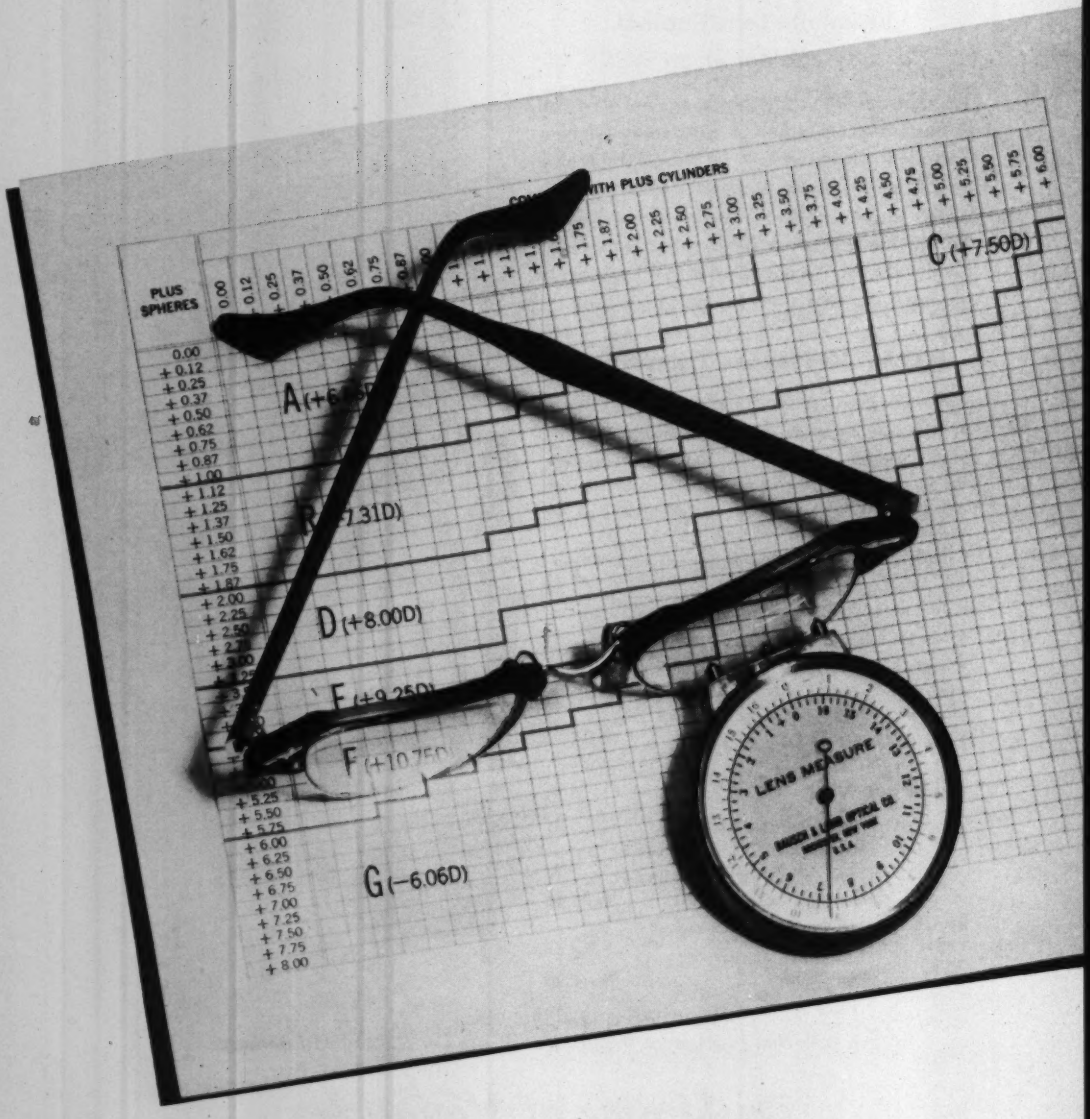
RIGHT because Gantrisin Ophthalmic Solution promptly and effectively controls a broad front of micro-organisms, including such common pathogens as *Hemophilus influenzae* (Koch-Weeks). There is little likelihood of bacterial resistance emerging. **GANTRISIN OPHTHALMIC SOLUTION** is stable, sterile and isotonic, buffered at the pH of tears...no stinging, no burning. **RIGHT** in common external eye disorders, such as "pink eye" and nonspecific conjunctivitis, punctate and dendritic keratitis, superficial corneal ulcers, blepharitis; *also* in ocular trauma, for prophylaxis following surgery and after removal of foreign bodies.

Consult literature and dosage information, available on request, before prescribing.

Gantrisin Diethanolamine Ophthalmic Solution and Ointment contain 4% Gantrisin® – brand of sulfisoxazole.

ROCHE
LABORATORIES
Division of Hoffmann-La Roche Inc.

Here's why you KNOW



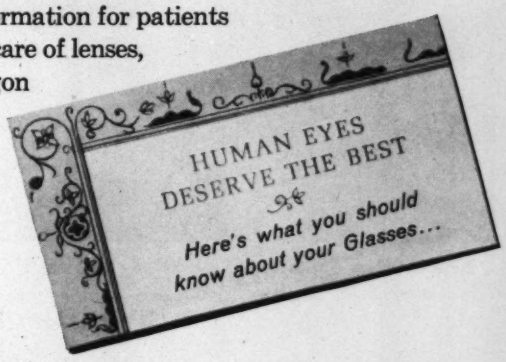
your patients are getting the quality of Orthogon lenses

There's no confusion about vision quality for your patients when you prescribe Orthogon marginally corrected lenses.

1 You *know* the exclusive benefits of the Orthogon system: not compromise correction, but correction for marginal astigmatism, the one aberration for which the human eye cannot compensate. The Orthogon principle of marginal correction is not a matter of manufacturing expedience; of changing correction factors in various ranges—a pinch of this and a pinch of that.

2 You always *know* when the prescription has been made in Orthogon. A Geneva lens gage reading confirms the standard base curve clearly shown on the Orthogon lens chart.

3 You also *know* that the patient knows he's getting the best. Every Orthogon prescription is delivered to you with the interesting miniature booklet, "Human Eyes Deserve the Best," which includes valuable information for patients on vision problems and the care of lenses, and a certification of Orthogon exclusive quality.



BAUSCH & LOMB
SINCE 1853

Upgrade to Orthogon...
the uncompromising standard

Patients 50 or over?
Rx: Univis CV Lenses

And 40 million people in the U. S. are 50 or over! Most of them wear prescriptions. Why not check your records? Many of your own patients are 50 or over. You provide them the finest Rx possible with Univis Continuous Vision® lenses. For professional information on fitting, patient demonstration and the *complete* line of Continuous Vision lenses, write Univis Professional Services Division.

UNIVIS INC., Vision Park, Fort Lauderdale, Florida

UNIVIS EXCELLITY

OMA BVI

AESTHETICS alone did not dictate the pleasing lines of the Gambs Slitlamp.

The inclination of the lamp housing and the microscope mounting evolved from consideration for the posture of the observer who using the instrument slightly bent forward was found to be the most comfortable approach.

The observation field of the microscope is uninterrupted by the passing of the lamp across the line of view. Concentric mounting of the two elements permits full viewing throughout the half circle of traverse and the use of any angle o to 180° between the light beam and the line of view.

Attention has been paid to the centering the weight of the instrument upon the point of rotation and thereby smoothness of movement is assured throughout.

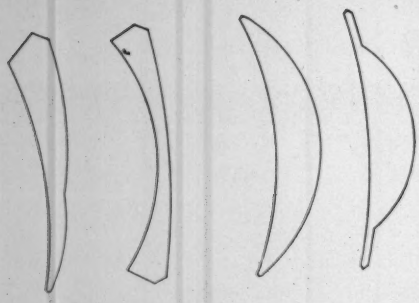
When using the available horizontal slit with the two arms co-incident the illuminating beam is projected from slightly below the line of viewing.

Since 1927 specialized experience in the design and production of ophthalmic instruments have impressed upon us the value of such attention to detail.

GAMBS
140, RUE MAZENOD
LYON
FRANCE

SLIT LAMP, complete with table and transf.
refer. 850 T : $ 875

Please write for fully descriptive literature of our products
SLIT LAMP — OPHTHALMOMETER — PERIMETER
TRANSLATING TABLES — ADJUSTABLE STOOLS



LIGHTWEIGHT TITMUS Cristyl®

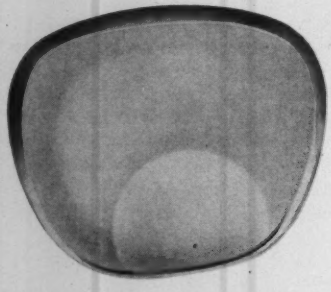
EXCELLENT FOR ANY FOCI!

Now for the first time you can get *any* Rx you need in Cristyl with prompt delivery assured by your local independent laboratory

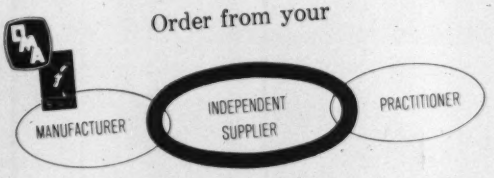
. . . BECAUSE

Titmus Cristyl Lenses are stocked locally in semi-finished form and, due to this new patented* material, can be finished by your local laboratory.

Specify Cristyl.



Order from your



"Golden Link" to Complete Service

TITMUS OPTICAL COMPANY, INC.
PETERSBURG, VIRGINIA

*Pat. No. 2,964,501

		FINISHED DESCRIPTION				BASE
		SPHERE	CYLINDER	AXIS	DECENTER	PRISM
DISTANCE	R	+100				8¾ D
	L					
			SEG. INSET	TOTAL	READING HEIGHT	INTER HEIGHT
ADDITIONS	R	+250	R 2MM		18	
	L		L			

PUPILLARY WIDTH READING:

DISTANCE:

UNIFORM DENSITY

*Sloan L. L.: New Test Charts for the Measurement of Visual Acuity at Far and Near Distances. American Journal of Ophthalmology, 48:807-813, (Dec.) 1959.

AMERICAN JOURNAL OF OPHTHALMOLOGY

SERIES 3 · VOLUME 52 · NUMBER 1 · JULY, 1961

CONTENTS

AMERICAN JOURNAL OF OPHTHALMOLOGY
VOLUME 52 JULY, 1961 NUMBER 1

USE AND MISUSE OF IRRADIATION IN LID MALIGNANCIES*

SIDNEY A. FOX, M.D.
New York

The choice of irradiation or surgery in the treatment of lid malignancies is a problem which frequently confronts the ophthalmologist. The object of this short paper is to report a number of cases of lid epitheliomas treated by irradiation or surgery or both. The discussion will be limited to the results of treatment by these two modalities. At some later date a more comprehensive paper will deal more extensively with such details as percentage incidence of the various types of malignancies, predilection for sites of involvement, surgical techniques, and so forth. The few cases reported here were chosen from a large series as typical of the varied problems involved and the results to be expected.

All cases represent long-standing neglect (from five to 20 years) by the patient and therapeutic problems for the ophthalmic surgeon. For the sake of brevity all but the most pertinent details have been omitted from the case reports.

CASE REPORTS

CASE 1

M. B., a 55-year-old man, gave a history of a lesion of the left lower lid which had been present for at least five years. Examination disclosed a large flat rodent ulcer which involved the medial two thirds of the left lower lid (fig. 1-A). Fortunately the lid margin was intact. Repair was made by total resection and immediate repair by free skin graft from the left upper lid (fig. 1-B). There has been no recurrence in 10 years.

CASE 2

R. D., a 69-year-old man, was seen in consultation and gave a history of an ulcerative lesion of the right lower lid and cheek which had been present and increasing in size for approximately nine years (fig. 2-A). Diagnosis was basal-cell carcinoma. It will be noted that, except for involvement of a much larger area, this case is essentially the same as the previous one. Hence a wide excision with plastic repair to be followed by irradiation later, if the pathologic report made it necessary, was advised. This advice was ignored and instead the patient subsequently received 23 X-ray treatments delivering a total of 6,900 r over a four-week period. The roentgenologist then felt that the area would heal itself and that no plastic surgery would be necessary.

Sixteen months later the irradiated area was still unhealed due to radiation necrosis and cicatricial lagophthalmos with ectropion and radiation keratitis had developed (fig. 2-B). In order to prevent further deterioration of the eye two attempts at repair were made by sliding and hammock flaps. Both failed. A conjunctival flap to cover the cornea melted away. The vision was now 20/100 and glaucoma with secondary cataract had developed. Finally, 30 months after irradiation, a forehead flap was raised, delayed a month, and then rotated down to cover the involved area. The donor area was filled in by a free graft. Healing was slow and six months later the eye had to be enucleated because of an intractable endophthalmitis. This man has been in and out of the hospital for over three years and has lost that much time from his job. So much for the claim that X-ray therapy keeps patients out of the hospital.

CASE 3

S. B., a 67 year-old-woman, reported a lesion of the right lower lid which had been present for eight years. Six years ago "some skin" had been removed but the lesion had recurred. Examination disclosed a rodent ulcer involving the outer half of the right lower lid (fig. 3-A). Repair was made by resection and sliding pedicle graft with good result (fig. 3-B). There had been no recurrence six years after operation when the patient was last seen.

CASE 4

F. M., a 70-year-old man, gave a history of a painless nonhealing ulcer of the right upper lid for the past seven years. Examination disclosed a deep rodent ulcer of the right upper brow and lid (fig.

* From the Department of Ophthalmology, New York University-Postgraduate Medical School. Presented at the VI Pan-American Congress of Ophthalmology, Caracas, Venezuela, February, 1960.

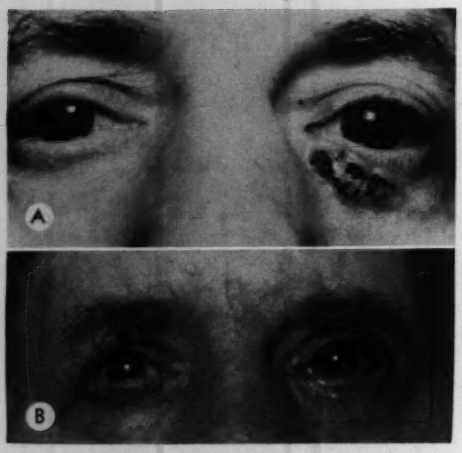


Fig. 1 (Fox). (A) Rodent ulcer of left lower lid. (B) Appearance after repair by free full-thickness skin graft.

4-A). Complete debridement was done and a temporal flap was swung down for temporary closure. The area was then treated with X-rays and received a total of 6,000 r in divided doses over a period of 40 days. Fourteen months later the left brow was split and the upper half was swung over to widen the right upper lid and restore the brow (fig. 4-B). The result is not too pretty but it is adequate and the eye is saved, with good vision. Three and a half years later there had been no recurrence.

CASE 5

R. G., a 63-year-old woman, gave a history of a "wart" of the right internal canthus which had appeared about 20 years previously. It became irritated by glasses and "began to run." Over the years she had had several (number unknown) treatments of X-rays and radium with recurrence each time. When first seen, the whole right lower lid was absent and infiltration was beginning to extend into the floor of the orbit (fig. 5-A). The whole area was debrided, covered by a hammock flap from below, and then irradiated with 7,000 r of deep X-rays in divided doses over a period of 34 days (fig. 5-B). Two years and four months later a hammock flap was raised in the upper lid and delayed but it turned black (fig. 5-C). A tubed flap will be tried next. The vision in the eye is down to 20/80.

CASE 6

A. C., a 62-year-old woman, gave a history of a lesion of the left internal canthus which first appeared eight years ago and had grown steadily larger (fig. 6-A). Repair was made by excision and skin graft from the left upper lid (fig. 6-B). Healing was rapid with good cosmetic result (fig. 6-C). The patient was lost to follow-up after 20 months at which time the appearance was excellent.

DISCUSSION

It will be noted that Cases 1, 3 and 6 which received no irradiation gave the best results. Case 4 in which primary surgery was supplemented by secondary irradiation also did well. Cases 2 and 5 in which primary irradiation was used have not done well, that is, the malignancy has been cured but the patient has not.

Admittedly in these latter cases the lesion was more advanced. However, I am convinced that had surgery with primary repair been performed in Case 2 before irradiation, as in Case 4, much of the cicatrization and resultant eye damage could have been avoided. Obviously Case 5 is a sad, neglected case in which irradiation had to be used to forestall deeper invasion of the orbit. A little surgery earlier in the disease would have saved a lot of later trouble.

As Reese[1] points out, any tumor growth can usually be arrested if a sufficient dose of

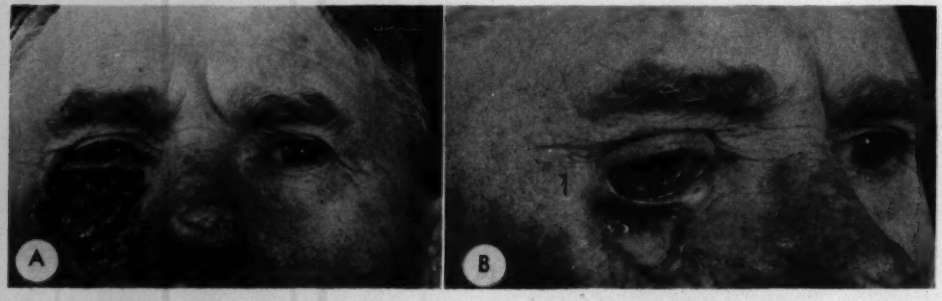


Fig. 2 (Fox). (A) Rodent ulcer of nine years' duration. (B) Radiation necrosis still present 16 months after X-ray therapy.

X-ray radiation is given. The cost, however, can be very high and, in some cases, prohibitive as shown in Case 2.

Briefly summarized the disadvantages of primary irradiation are:

1. Completeness of extirpation is uncertain.

2. Adequate biopsies are difficult to obtain because of occasional variations in cell structures in different parts of the neoplasm, hence the radiotherapist sometimes has to work blindly as pointed out by Stallard[2] and others.[3,4]

3. Irradiation may cause atrophy, painful scarring and indolent ulceration of the skin due to radiation necrosis (Case 2). Frequently resulting conjunctival keratoses may keep the eye red and irritated indefinitely. In cases involving the medial canthus, irradiation can easily occlude the puncta and canaliculi. It has also been known to cause keratitis, iridocyclitis, secondary glaucoma, cataract and even loss of the eye.

4. Recurrence after irradiation, which is more frequent than after surgery, requires even greater amounts of X-rays.

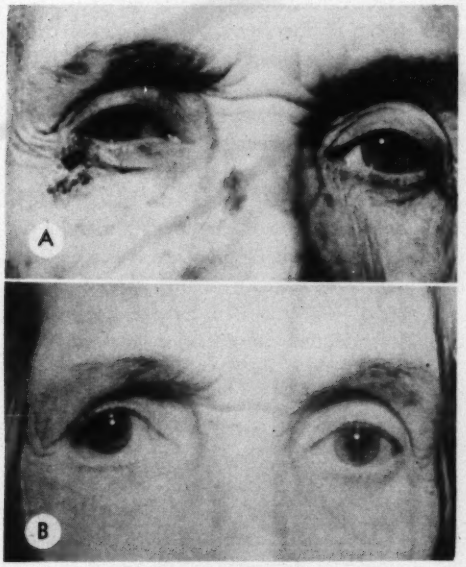


Fig. 3 (Fox). (A) Basal-cell tumor of right lower lid. (B) Appearance after repair by sliding pedicle graft.

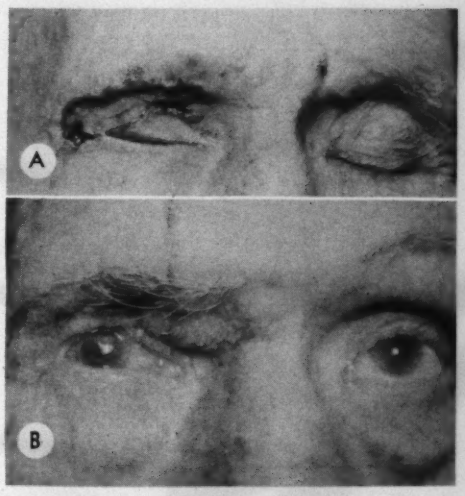


Fig. 4 (Fox). (A) Basal-cell epithelioma of right brow and lid. (B) Appearance after debridement, irradiation and repair by pedicle grafts.

5. Perhaps most important of all is the fact that irradiation vitiates tissues and blood supply so much that postradiation surgery becomes a formidable problem even if postponed for several years (Case 5). Free grafting is difficult and one must resort to tubes and pedicles with their inevitable scarring and disfigurement in order to get healing. Even then healing is difficult and slow (Case 2).

Primary irradiation is a must only in old neglected cases where life is at stake and where surgery would obviously be too little and too late and hence of no value, as in Case 5. Another use of irradiation is as an adjunct to surgery after primary surgical repair (Case 4).

Primary surgery, on the other hand, offers the ophthalmologist a choice of many methods and procedures of repair: the free graft, the sliding graft, the rotated pedicle, the tubed graft, and so forth. Hence all in all, barring a hopeless condition where life is involved (and such cases are rare in ophthalmology) primary surgery rather than irradiation would seem to be by far the best choice for patient and surgeon. It offers a more certain diagnosis, less scarring, better functional and cosmetic result, surer eradication of the

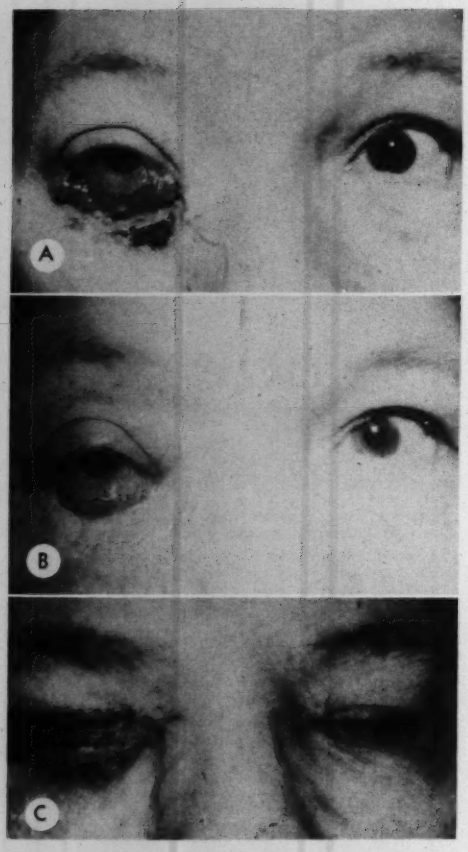


Fig. 5 (Fox). (A) Infiltrating epithelioma of right lower lid. (B) Appearance after debridement, irradiation and hammock flap repair from below. (C) Delayed hammock flap raised from upper lid turns black due to radiation.

lesion and hence less chance of recurrence.

The object of this paper is not to condemn the use of irradiation but to argue against its misuse.

There is at present a great controversy as to the best method of treating lid epitheliomas. The radiologist and his cohorts are certain that the ideal modality is irradiation. Opposed are those who feel that surgery is the best procedure in most cases. There are many papers in the literature which seem to prove that both sides are right.

It occurs to me that one of the main causes of this impasse is that terms have not been properly defined and that the frames of reference vary widely. What is a cure? For a roentgenologist a cure is getting rid of the cancer. For the ophthalmic surgeon this is simply a preliminary step in the cure (Cases 2 and 5) and a final cure is attained only when the patient has been restored as near as possible to his previous cosmetic state.

It is this difference of definition which is probably one of the main causes of disagreement. Admittedly, if the lesion is small and away from the margin either modality, irradiation or surgery, may be used and the lesion cured. But the larger lesions which require surgical repair after a "cure" by irradiation are the ones that always give trouble and this is why surgeons who are interested in the final appearance of their patients feel that irradiation, which makes surgery long delayed, more difficult and sometimes almost impossible, should be used cautiously and then only if there is no other recourse.

Summary and Conclusions

1. In six cases of long-neglected lid epitheliomas excellent cosmetic results were obtained in three cases in which surgery alone was used.

2. An adequate result was obtained in a

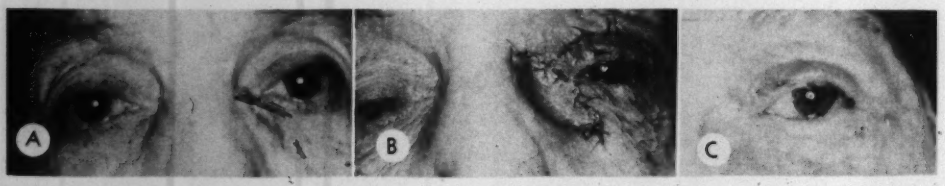


Fig. 6 (Fox). (A) Basal-cell epithelioma of left internal canthus. (B) Repair by full-thickness free skin graft. (C) Appearance after repair.

fourth case where surgical debridement and primary repair were followed by irradiation and definitive surgical repair.

3. The two cases in which irradiation was used initially showed poor results.

4. Primary irradiation may be needed as a life-saving measure. Secondary irradiation may be necessary in long-standing neglected cases as an adjunct to surgery.

5. If a choice exists, surgery is the modality to be selected.

11 East 90th Street (28).

References

1. Reese, A. B.: Tumors of the Eye. New York, Hoeber, 1953, p. 8.
2. Stallard, H. B.: Treatment of malignant neoplasms of the eyelids. Brit. J. Ophth., **43**:159-168 (Mar.) 1959.
3. Cogan, D. G., et al.: Symposium: Ocular effects of ionizing radiation and radiotherapy. Tr. Am. Acad. Ophth., **63**:429-497 (July-Aug.) 1959.
4. Leahey, B. D.: Beta radiation in ophthalmology: Indications, technique and complications. Am. J. Ophth., **49**:7-28 (Jan.) 1960.

ON THE GOLDEN ANNIVERSARY OF SLITLAMP MICROSCOPY*

James E. Lebensohn, M.D.
Chicago, Illinois

Just a half-century ago, on August 3, 1911, Allvar Gullstrand demonstrated the first slitlamp before the German Ophthalmological Society at Heidelberg. Three years earlier, while investigating the dioptrics of the eye, for which he received the Nobel Prize later in 1911, Gullstrand sought a method by which the posterior curvature of the cornea could be sharply observed. An accurately focused slit of concentrated uniform illumination was necessary. He selected the rod-shaped filament of the Nernst lamp as the source and concentrated the rays with a doublet of planoconvex lenses of 22D. power, curved surfaces adjacent, placed so that the first lens was at its principal focal distance from the filament and the second lens at its principal focal distance from the slit. Using a plus 14D. aspherical hand lens, the element now termed the illuminating lens, he focused the beam of the slit precisely on the ocular structure under study which he scrutinized with telescopic spectacles. Further clinical use of the slitlamp confirmed his conviction that focal illumination of the image of the source of light provided more intense and homogeneous light than could be obtained directly from the light source and thus rewarded the observer with details not otherwise perceptible (fig. 1). As a consequence, Gullstrand was the first to describe the fibrillar structure of the vitreous in the normal living eye.

The microscopic study of the living eye had previously proved futile. In 1893, Abbe produced with Porro prisms the binocular field glass. The principle was extended to the binocular microscope by Greenough, an American zoologist. In 1897 Czapski devised a corneal microscope by mounting Greenough's instrument horizontally, adjusting the focus and attaching an illuminating bulb. With this illumination, however, the corneal microscope was of little value. Said Laqueur: "Whatever can be seen by its means can be seen more easily and surely with the binocular corneal loupe."

Henker launched the prototype of the modern slitlamp apparatus in 1916 when he rescued the Czapski microscope from oblivion by joining it to the Gullstrand illuminating system, which he placed with its

* From the Department of Ophthalmology, Northwestern University Medical School.

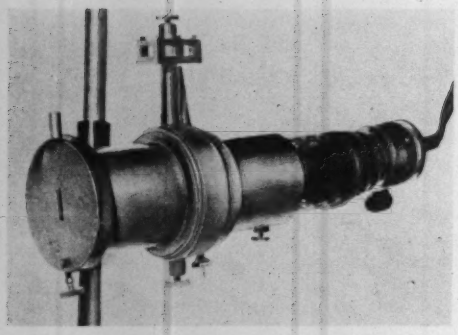


Fig. 1 (Lebensohn). Gullstrand's slitlamp illuminating unit. (From Berliner, M.: *Biomicroscopy of the Eye*, Volume 1.)

illuminating lens on a swinging arm, and provided adjustments for the ready manipulation of the two elements.

Research by Vogt

Alfred Vogt promptly perceived the vast potential of this workable arrangement and his pioneer discoveries in slitlamp microscopy are reminiscent of the accomplishments of von Graefe with the ophthalmoscope and of Galileo with the telescope. Vogt amplified the investigative possibilities of the slitlamp by making the slit adjustable, changing the optical arrangement, and varying the methods of illumination. After the end of World War I, the Nitra lamp, a nitrogen-filled bulb with a coiled tungsten filament, superseded the discontinued, more expensive and less durable Nernst lamp, but with Gullstrand's optical arrangement the Nitra lamp produced a helical image in the slit. Fortunately, the formation of homogeneous light from such a source had been solved by Köhler in 1893. Thus guided, Vogt, in 1920, focused the image of the filament on the posterior surface of the illuminating lens. As compared with the Nernst lamp, the resulting beam was equally homogenous and 50-percent more luminous. He also lengthened the focus of the illuminating lens, changed its shape to that of a narrow rectangle, and dispensed with its aspherical form which he found unnecessary. Vogt's accurate observations revealed an unsuspected frequency of embryologic rudiments and many new evidences of ocular senility.

Vogt's career began with the private practice of ophthalmology in the town of Aarau, Switzerland, near which he was born. There, in independent research, he proved the susceptibility of the crystalline lens to prolonged infrared radiation; and introduced ophthalmoscopy by red-free light. In 1918, Vogt made the unprecendented transition from private practice to the academic appointment of professor of ophthalmology at the University of Basle and, in 1923, he accepted the invitation to head the Ophthalmic Institute of the University of Zurich. Though the range of his interests covered all ophthalmology, Vogt's researches centered on the slitlamp. He demonstrated the value of each method of illumination. The thin optical section produced by a narrow beam allowed an accurate determination of depth within the media and yielded new insight in the topography of the crystalline lens. Retroillumination revealed vacuoles in the lens, corneal edema and keratic precipitates, while specular reflection brought out the endothelial mosaic on the posterior corneal surface and the polychromatic luster at the posterior pole of the lens in early cataracta complicata. The scattering of light by suspended particles so enhanced discrimination that cells in the aqueous were visible with the standard magnification of ×23. The ultramicroscope devised by Siedentopf and Zgismondy, in 1903, utilized the Tyndall effect similarly and by its means particles of colloidal gold have been detected as minute as 17 Å.U. or 1/250 the wavelength of blue light.

In 1920 Vogt gave the first international slitlamp course, consisting of six to eight hours daily for a week, for which the zealous student paid 20 Swiss francs. The first edition of his *Atlas of Slitlamp Microscopy* (1921) and the three-volume second edition (1930-1940), completed only three years before his death, rank among the great creative books of ophthalmology. Vogt and his disciples added to the lexicon of oph-

thalmology a technical slitlamp vocabulary that included the terms bedewing, luster, optical section, retroillumination, and indirect lateral, diffuse, oscillating and specular illuminations. In 1925, Mawas suggested the word biomicroscopy as a succinct equivalent for the phrase, slit-lamp microscopy of the living eye.

Advances by Koeppe and Goldmann

Another genius who advanced slitlamp microscopy was Leonhard Koeppe. For more than a decade his "universal slitlamp" was a favorite model (fig. 2). He introduced the blackened Koeppe tube between the slit and the illuminating lens to absorb annoying scattered light. At the suggestion of Koby a plano-convex cylinder, 9.0D. axis 180, was set in the tube so as to triple the length of the beam and permit observation of the entire cornea and lens. In 1918, Koeppe successfully extended slitlamp microscopy to the fundus. Though his technique was cumbersome and difficult, he demonstrated that the essential requirements were nullification of the refractive power of the eye and reduction of the observation-illumination angle to to five degrees so that their axes intersected far enough back. The Koeppe contact lens satisfied the first requisite but meeting the second was the troublesome problem. The substitution of Goldmann's reduction prism for the mirror of Koeppe proved the adequate solution and resulted in remarkable progress in this field. Lemoine and Valois, in 1923, demonstrated that a plano-concave lens of 55D. placed before the observed eye was a feasible alternative to the Koeppe lens. A similar precorneal lens, contrived by Hruby in 1941, is now a standard slitlamp accessory, and is particularly advantageous in the examination of children or sensitive patients, and of diseased, injured or recently operated eyes. The contact lens, however, gives a sharper image and a larger field. In 1932, Evans applied the principle of indirect ophthalmoscopy to the slitlamp; the microscope enlarged the aerial image formed by the precorneal convex lens. In 1953, Bayadi

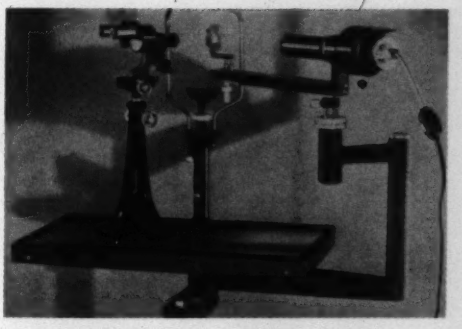


Fig. 2 (Lebensohn). Koeppe's universal slitlamp, simplified adaptation. (Bausch and Lomb Optical Company.)

revived the idea, using a planoconvex lens of 60D. The Bayadi lens, now available as a slitlamp accessory, is particularly indicated in the examination of high myopes. The prerequisites for examination of the deep vitreous are a Koeppe-type contact lens or the Hruby lens, a maximally dilated pupil and the largest possible observation-illumination angle.

Koeppe was the first to extend the use of the slitlamp to gonioscopy but the perfected simplified technique in current practice is Goldmann's achievement. In 1938 Goldmann devised a contact lens that contained a mirror at an angle of 62 degrees with the front flat surface which reflected the image of the angle. Rotation of this contact lens brought all meridians into view, the mirror being placed opposite the segment under scrutiny. In the recent technique a narrow slitbeam is employed while the slit and the mirror are rotated to vertical, oblique or horizontal positions as these respective segments are successively explored. For vertical and oblique segments the observation-illumination angle is 10 degrees, but for the horizontal segment the angle is shifted to zero and the horizontal slit is inclined about its axis 10 to 15 degrees. The magnification of $\times 10$ to $\times 16$ is generally most useful.

Goldmann's interest in tonography prompted him to search for an accurate method of registering ocular tension that would not be influenced by variations in ocu-

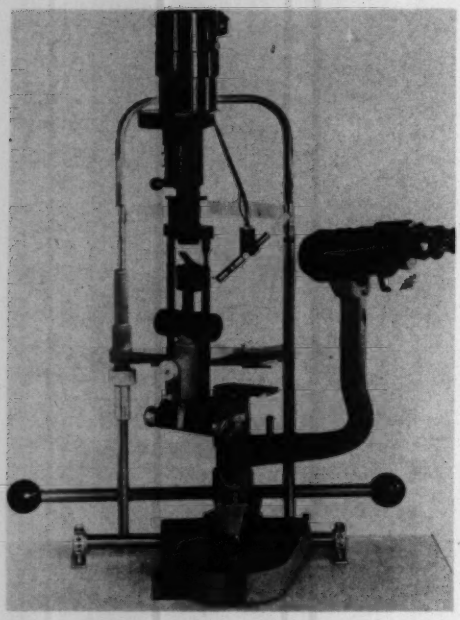


Fig. 3 (Lebensohn). Goldmann's latest design: Haag-Streit slitlamp 900.

lar rigidity and corneal curvature. The brilliant solution, announced in 1955, was the slitlamp application of applanation tonometry—a sublimation of the almost forgotten device conceived by Fick of Zurich in 1888. As the surface flattened by the Goldmann applanation tonometer is three mm. in diameter and causes a volumetric displacement of only 0.56 mm.^{3}, the pressure measured is practically identical with the actual intraocular pressure.

Further progress

Ulbrich's drum is frequently used for the measurement of depth. This micrometer screw, fixed to the microscope, registers to 0.1 mm. the displacement in focusing. A more accurate measurement of the thickness of the cornea and the depth of the anterior chamber is possible with a recent depth micrometer mounted on the corneal microscope that uses the coincidence method and consequently gives results independent of the motion of the patient's eye. The readings are influenced, however, by the curvature of the cornea which must be previously determined.*

The slitlamp also provides a delicate test of the pupillary reaction to light as well as means to determine pupillary disturbances of a hemianoptic nature. For the first test a ground-glass filter is inserted; the slit is closed and opened suddenly to its full width. The second test requires a Hruby lens before the eye and a slit as narrow and short as possible. With the light spot directed to the desired position of the retina, the width of the slit is widened and the pupil observed as the movement of the hand places the light off and on.

Comberg, in 1933, endowed the slitlamp and microscope with a common axis of rotation; by tightening a coupling both turned together and maintained the slit-image constantly in the field of view. The Goldmann slitlamp, exhibited in 1937, embodied in addition a fixation lamp, a steering lever by which the apparatus could be moved precisely and a reduction prism that could be placed when needed in front of the illuminating lens. With this instrument the fundus and deep vitreous were accessible to examination as well as the anterior segment. Goldmann's three-mirror contact lens added further versatility; its clear central zone served for the study of the posterior pole, while the mirrors rendered gonioscopy possible and brought into view the middle and peripheral zones of the fundus and vitreous. The employment of viscid two-percent methylcellulose as the fluid facilitated handling, since the liquid does not drip out while inserting the contact lens and air bubbles are rapidly removed by simply tilting and turning.†

---

* The use of Lobeck's split field ocular is beautifully illustrated by G. M. Bleeker (Arch. Ophth., **65**:369-374 [Mar.] 1961) and described also by D. Donaldson (Am. J. Ophth., **51**:714 [Apr.] 1961).

† Further advances have been attained in the low vacuum diagnostic contact lenses designed by J. G. F. Worst and K. Otter (Am. J. Ophth., **51**: 410-424 [Mar.] 1961).

At the International Congress of Ophthalmology of 1958 the slitlamps shown by the various manufacturers presented a novel appearance, as well as advantages that made all previous models outdated (fig. 3). To reduce light reflexes every component of the optical system was coated with magnesium fluoride. The objectives in the turret were automatically correctly focused on changing magnification. The illuminating system contained a terminal reversing prism, all embodied in a freely movable vertical shaft that permitted the illumination-observation angle to be varied from 90 degrees to zero. The slit-image, now more brilliant, could be freely rotated to any angle, and in the horizontal meridian could be inclined about its axis as much as 20 degrees. Incidentally, the modernized apparatus with its desirable accessories has reached a new high in cost, approximating $2,000.00. Nevertheless, the demand is such that orders for the favorite model cannot be delivered for one to two years.

Current role of biomicroscopy

From the conjunctiva to the fundus the slitlamp has added a new perspective to the study of the living eye. Rüedemann, in 1933, suggested scrutiny of the conjunctival vessels whenever vascular disease was suspected. Even in the absence of general vascular disease, varicosities and telangiectases are common, especially among the aged, and their rupture is the usual cause of nontraumatic subconjunctival hemorrhage. In various conditions, such as myocardial disease, malaria, traumatic shock and hypotherma, the pericorneal and conjunctival blood vessels show intravascular red-blood-cell sludging. Such sludging is usually accompanied by an increase in erythrocyte sedimentation rate. In angiography, the intravenous injection of concentrated iodinated radiopaque media rapidly causes this vascular alteration, which is generally resolved after 20 minutes. In 1942, Karl Ascher, then at the University of Cincinnati, published a study of the vasculature near the limbus which revealed aqueous veins intercalated between Schlemm's canal and the episcleral and conjunctival veins—a discovery which definitely proved that the aqueous was in continuous circulation. The visible aqueous veins varied from a fraction of a mm. to one cm. With the increasing popularity of corneal contact lenses, the biomicroscope has given ophthalmologists the most percise means of evaluating both fit and tolerance.

Biomicroscopy frequently establishes a diagnosis not otherwise possible. Burki in 1940 noted the slitlamp appearance of cystine deposits in the cornea and conjunctiva as an early pathognomonic sign of cystinosis, a metabolic disorder of infants; and in 1955 observed that some patients with multiple myeloma show both corneas studded with iridescent crystals a few years before the systemic disease is medically diagnosed. Minute colorless foreign bodies of glass or plastic as well as slight opacities of the media may be undetectable by other means. The depth in the cornea of a wound, scar or foreign body can be definitely ascertained with the narrow beam. Only the slitlamp can reveal the first signs of many diseases as evidenced, for example, in the disintegration of the endothelial mosaic in Fuchs' dystrophy, a few keratic precipitates in cyclitic glaucoma, flare and cells in the aqueous in sympathetic ophthalmia and polychromatic luster at the posterior pole of the lens in cataracta complicata. Atrophy of the lens is revealed by progressive obscuration of the bands of discontinuity. After cataract extraction or subluxation of the lens biomicroscopy resolves whether vitreous has entered the anterior chamber.

With the aid of stereoscopic slitlamp examination, hemorrhages and exudates in the fundus can be precisely localized and retinoschisis, posterior detachment of the vitreous and very flat detachments of the retina are more certainly diagnosed. Likewise it facilitates the differentiation of a macular cyst from a macular hole, and at-

tenuated parts of the retina from retinal holes. A slitlamp feature of central serous retinopathy is an umbilical depression at the fovea, giving the optical appearance of a cupid's bow. Slitlamp microscopy discloses in papilledema differences in level as definitely as Gullstrand's binocular ophthalmoscope, and distinguishes papillitis from papilledema by fine precipitates on the posterior surface of the vitreous or the Tyndall phenomenon in the space in front of the disc.

The contemporary culmination in the contruction and use of the slitlamp is a tribute to the tempo of progress in the past 50 years. In contrast is the four-century span that elapsed between the introduction of movable type by Gutenberg and Hoe's fabrication of the rotary press in 1847. No period has been so advantageous to the young ophthalmologist as the present. The older specialist realizes, vaguely or clearly, that he is being gradually outmoded by the rapid innovations in technique and instrumentation. The spectacular evolution of biomicroscopy as an essential tool of ophthalmic practice is intimately interwoven with this recent and amazing progress.

4010 West Madison Street (24).

References

Ascher, K. W.: Aqueous veins. Am. J. Ophth., **25**:31-38 (Jan.) 1942.

Berliner, M.: Biomicroscopy of the Eye. New York, Hoeber, 1943, v. 1; 1949, v. 2.

Busacca, A., Goldmann, H., and Schiff-Wertheimer, S.: Biomicroscopie du corps vitré et du fond de l'oeil. Paris, Masson & Cie., 1957.

Doggart, J. H.: Ocular Signs in Slit-Lamp Microscopy. St. Louis, Mosby, 1949.

Duke-Elder, S.: Textbook of Ophthalmology. St. Louis, Mosby, 1938, v. 2, pp. 1134-1152.

———: Recent Advances in Ophthalmology. St. Louis, Mosby, 1951.

Hruby, K.: Slitlamp microscopy of the posterior section of the eye with the new preset lens. Arch. Ophth., **43**:330-336 (Feb.) 1950.

Koby, F. E.: Summary of Microscopy of the Living Eye. Philadelphia, Blakiston's, 1925.

Stocker, F. W.: Prof. Alfred Vogt. Arch. Ophth., **31**:172-174 (Feb.) 1944.

Thomas, C. I.: The Cornea. Springfield, Ill., Thomas, 1955.

ASYMMETRIC PROPTOSIS*

Richard O. Schultz,† M.D., Richard D. Richards, M.D., and Henry E. Hamilton, M.D.

Iowa City, Iowa

Reported statistics on the etiology of unilateral exophthalmos have varied according to the diagnostic methods used and the specialty group conducting the study.

A recent radiologic survey by Bullock and Reeves of 138 cases revealed that mucocele was the commonest cause of unilateral exophthalmos.[1] This diagnosis was made in approximately 12 percent of cases. The second, third, and fourth most common lesions were inflammation, carcinoma of the sinus, and meningioma. Endocrine causes for exophthalmos were seen in only two percent of cases. The largest group of all were the undiagnosed cases which made up almost 18 percent of their total.

Van Buren and Poppen from the Neurosurgery Department of Lahey Clinic listed the findings in 86 orbital explorations performed because of unilateral exophthalmos.[2] The commonest cause in that series was meningioma 31 percent; carotid aneurysms and fistulas were second with approximately 12 percent and the third most common cause of asymmetric proptosis was fibrous dysplasia

* From the Departments of Ophthalmology and Internal Medicine, College of Medicine, University of Iowa.

† Present address: Phoenix Indian Hospital, U. S. Public Health Service, Phoenix, Arizona.

of bone. Endocrine exophthalmos in this series also comprised about two percent of cases.

Drescher and Benedict at the Mayo Clinic reviewed 177 patients with asymmetric proptosis and found 43 percent non-neoplastic, 44 percent neoplastic and 13 percent undiagnosed.[3] Of all causes, endocrine exophthalmos was the most common with approximately 23 percent of cases; meningiomas comprised 12 percent and hemangiomas 10 percent.

O'Brien and Leinfelder reported 82 consecutive patients with unilateral exophthalmos seen at the State University of Iowa Hospitals.[4] The most common cause was orbital abscess (15 cases). Cellulitis was next most common with 13 cases and there were three cases of osteomyelitis and periostitis to complete the inflammatory group of 31 cases. Of the 51 noninflammatory cases, there were 24 malignant neoplasms. Included were nine carcinomas, six primary and three metastatic; eight sarcomas, five primary and three metastatic; and seven metastatic tumors of the hematopoietic system. There were 10 benign neoplasms consisting of four meningiomas and one each of glioma of the optic nerve, adamantinoma, chondromyxoma, cavernous hemangioma, neurofibroma, and pseudotumor. There were three mucoceles. Eight cases were due to trauma and included four hematomas, three carotid cavernous fistulas and one emphysema. There were only two cases of endocrine exophthalmos. In one case, unilateral axial myopia was the cause for the asymmetric proptosis. In three patients, the reason for the asymmetric proptosis was not determined.

TABLE 1

ASYMMETRIC PROPTOSIS

(59 cases, 1955 to 1960)

Cause	Cases
Endocrine exophthalmos	21 (36%)
Orbital tumors	18 (31%)
Inflammation	6 (10%)
Pseudotumor	5 (8%)
Undiagnosed	4
Carotid-cavernous fistula	2
Mucocele	1
Injury	1
Developmental	1

TABLE 2

ORBITAL TUMORS

(18 cases, 1955 to 1960)

Tumor	Cases
Lymphoma	4
Lacrimal gland tumors	3
Sarcoma	3
Gliomas of optic nerve	2
Metastatic adenocarcinoma	1
Nasopharyngeal carcinoma	1
Mengioma—sphenoid ridge	1
Angiofibroma	1
Lymphangioma	1
Dermoid	1

The present study was undertaken for the purpose of comparing the causes of unilateral exophthalmos seen from 1955 to 1960 with those reported in 1934 and to determine what percentage of cases could be diagnosed by careful clinical examination, radiologic and endocrine studies.

RESULTS OF STUDY

In the five-year period of 1955 to 1960, 59 cases of asymmetric proptosis were seen at the University Hospitals (table 1). Only those patients with a difference of three mm. or more, as measured by a Hertel-type exophthalmometer, were included in the series.

There were only six (10 percent) inflammatory cases of which four were due to cellulitis, one was caused by osteomyelitis secondary to a retained foreign body, and one was due to cavernous sinus thrombosis. The distribution of inflammatory lesions was similar but the total number much less than the 31 cases in O'Brien and Leinfelder's series.

We had 53 noninflammatory cases and O'Brien and Leinfelder had 51. Although the total numbers are very similar, the distribution was markedly different. Endocrine exophthalmos was the most common cause of unilateral proptosis in our series, comprising 21 or 36 percent of all cases. Orbital tumors

comprised the next largest group, totaling 18 or 31 percent.

The orbital tumors are listed in Table 2. There were four metastatic hematopoietic tumors (three leukemic lymphomas and one reticulum cell lymphoma), three lacrimal gland tumors, three sarcomas (a fibrosarcoma probably arising from the frontal sinus, a malignant mesenchymal tumor arising in the area of the floor of the orbit, and an undifferentiated round cell sarcoma from the orbit), two gliomas of the optic nerve, one metastatic adenocarcinoma from the rectum, one nasopharyngeal carcinoma, one sphenoidal ridge meningioma, one nasopharyngial angiofibroma, one lymphangioma, and one dermoid.

The rest of the cases in the noninflammatory group consisted of five pseudotumors (eight percent), two carotid cavernous fistulas (three percent), one mucocele, one injury and one unilateral axial myopia. The cause of the asymmetric proptosis was not determined in four patients.

All patients with orbital tumors had positive findings by X-ray examination or physical examination, in addition to unilateral proptosis, which suggested the diagnosis of orbital tumor and which led to surgery. X-ray films were diagnostic in three of the cases and 13 showed some radiologic changes, leaving only five with no X-ray change at all. In addition to the unilateral exophthalmos, all except one patient had clinical findings which helped make the diagnosis of tumor. These changes included decreased vision, palpable tumor mass, field changes, and fundus changes which consisted of papilledema or optic nerve atrophy, traction lines in the retina associated with pigment changes, and congestion and tortuosity of the retinal vessels. The one patient who had no clinical findings other than unilateral exophthalmos had orbital changes on X-ray examination which were diagnostic of a dermoid.

The patients with asymmetric proptosis on an inflammatory basis also had X-ray changes as well as histories and physical signs which were helpful in making a diagnosis. Three of the four cases of orbital cellulitis demonstrated an associated sinusitis on the roentgenograms. The fourth patient had a history of squeezing a pustule which was followed by orbital cellulitis. All four had elevated white blood counts and fevers. X-ray changes were found in a patient with a retained foreign body (wood) in the orbit for three years and showed a sclerosing osteomyelitis. The one patient with cavernous sinus thrombosis presented the typical physical findings and history, with onset of fever and chills progressing rapidly to high fever and comatose state accompanied by sudden unilateral exophthalmos with boardlike edema and oozing blood serum, dilated pupil and loss of light perception.

The rest of the patients in the series did not have any orbital changes visible on X-ray examination. They did have physical findings in addition to the exophthalmos. Two of the five patients with pseudotumor had a palpable orbital mass. One of these patients had a clinical diagnosis of endocrine exophthalmos and then developed a palpable mass four months later. Microscopic examination of tissue from this mass was consistent with pseudotumor. The second patient with a palpable orbital mass and a third patient without a palpable mass also had orbital tissue biopsied, and in both the diagnosis after microscopic examination was pseudotumor. All three patients had diplopia due to extraocular muscle involvement early and all three had papilledema at one time in the course of the disease. Two of these patients also had decreased vision in the involved eye due to secondary optic nerve atrophy and one developed a pseudotumor later in the second eye. The remaining two patients had a clinical diagnosis of pseudotumor. Both had diplopia as an early symptom and one patient had decreased vision followed by involvement of the second eye. The orbital tissue was not biopsied in either case.

There were two cases of carotid cavernous fistula and both occurred in women

over the age of 60 years. The clinical picture was typical in both with relatively sudden onset of a pulsating exophthalmos with a bruit and typical Medusa-head dilatation of the conjunctival vessels. One was confirmed by angiography. The other was in a 92-year-old woman and further diagnostic measures were considered dangerous.

There was one patient with asymmetric proptosis due to a local injury to the globe 53 years previously.

In one patient, asymmetric proptosis was due to progressive axial myopia of 20 diopters. A complete work-up, including thyroid function tests, skull and orbital X-ray films, spinal tap, CBC, EEG and angiograms, was negative.

The four undiagnosed cases included one patient with a soft tissue mass seen on X-ray examination but not found on orbital exploration. One had a history of proptosis for 20 years and, as did the other two, had negative clinical and laboratory findings. None of the four had a complete endocrine work-up including a Werner's test.

Discussion

Endocrine exophthalmos was the diagnosis in 21 of our 59 cases (36 percent) and comprised the largest group in our series. Therefore, the characteristic features of unilateral endocrine exophthalmos are elaborated upon in the following paragraphs:

A. Laboratory findings

Thyrotoxicosis is not the sine qua non for the diagnosis of endocrine exophthalmos. The exophthalmos reported in a large series of patients with thyrotoxicosis was typically bilateral (Hamilton[5] and Schultz[6]). In spite of the observation that an eye may protrude six to eight mm. during the course and treatment of Graves' disease, differences between the two eyes did not at any given time exceed 2.5 mm. (Hamilton[5]). In contrast to this, the endocrine exophthalmic patient without clinical thyrotoxicosis *may* show symmetrical protrusion but typically it is asymmetrical. Differences in measurements of the two eyes in our 21 patients ranged from three to eight mm.

On what basis, then, can the diagnosis of endocrine exophthalmos be made?

Werner reported on a series of euthyroid patients with early signs of Graves' disease but without clinically evident manifest thyrotoxicosis.[7] He noted that in such patients the effects of tri-iodothyronine on thyroidal uptake of radioactive iodine was atypical. In a normal euthyroid person, the oral administration of 50 μg. per day of tri-iodothyronine would depress the 24-hour uptake of I^{131} by 50 percent or more. In the patients with clinical signs of Graves' disease, however, tri-iodothyronine either had no effect on the 24-hour uptake of I^{131} or reduced it less than 50 percent. The test identified persons who had an abnormal thyroid pituitary relationship and it has become useful in evaluating endocrine exophthalmos in seemingly euthyroid patients. In our series Werner's test was done on 18 patients. It was negative in four patients. These were the patients with reticulum cell sarcoma, glioma of the optic nerve, and two patients with lacrimal gland tumors. It was positive in 14 patients and these patients had a clinical diagnosis of endocrine exophthalmos.

In our series, then, the Werner's test was positive in unilateral endocrine exophthalmos and negative in histologically proven orbital neoplasms. The Werner's test, therefore, can provide very significant information in the evaluation of unilateral exophthalmos and in some instances can obviate surgical exploration of the orbit.

To emphasize this, the following history is presented:

A 49-year-old woman had the onset of proptosis of the left eye in November, 1957, with associated periorbital edema and headaches. The onset of diplopia occurred two months later. Because of progressive proptosis of six mm. and diplopia with associated headaches, a craniotomy was done six months later. The orbit was unroofed at this procedure and orbital tissue obtained which was normal on microscopic examination. After surgery, the proptosis was noted to be pulsating and subsequently angiograms

and ventriculograms were done which were also negative. A family history of exophthalmic goiter was finally obtained and the patient put on large doses of thyroid extract for several months. She was referred to the University Hospitals in March, 1959.

Examination showed marked unilateral lid retraction and periorbital edema of the left eye. The inferior oblique and superior recti muscles were paretic with 10 degrees of left hypotropia. Exophthalmometric readings were 19, O.D., and 25, O.S., and the exophthalmos was pulsating. However, there was no bruit over the left eye.

I^{131} uptakes were 9.0 and 10 percent and she was placed on tri-iodothyronine (50 μg. per day). The I^{131} uptakes were repeated after one week of therapy and were essentially unchanged, constituting a positive Werner's test. This patient had normal visual acuity, normal fields, and ophthalmodynamometry readings were equal in each eye.

On the basis of the Werner's test and the observation of other components of the endocrine eye lesion (Hamilton[5]), a diagnosis of endocrine exophthalmos was made and she was continued on tri-iodothyronine. Vertical prisms were prescribed which relieved the diplopia and headaches. The measured proptosis remained essentially the same.

B. Clinical findings

Certain clinical features also characterize unilateral proptosis which is related to endocrine dysfunction. In spite of remarkable anatomic distortion, there is rarely any interference in visual function; visual acuity, fields, and fundi were normal in almost all of our cases. In contrast to this, tumors in the muscle cone—such as gliomas, meningiomas, and neurofibromas—can produce hyperopia, retinal striations, unusual field defects, and papilledema.

Extraocular muscle paresis occurred in two-thirds of our cases and was related to the degree of proptosis, as opposed to endocrine ophthalmoplegia related to thyrotoxicosis (Schultz[8]). Pseudotumors, lacrimal gland tumors and metastatic lesions are likewise frequently associated with palsies of the extraocular muscles.

Displacement of the globe is usually limited to a downward rotation, whereas true displacement of the eye is frequently seen with lacrimal gland tumors and mucoceles. In this connection there is no palpable mass in endocrine exophthalmos, whereas up to 60 percent of pseudotumors present a palpable mass (Iliff[9]).

The age range of our patients with unilateral endocrine exophthalmos was 17 to 54 years with approximately equal sex distribution. Unilateral exophthalmos in a child is therefore more likely to be due to such lesions as angiomas, gliomas, dermoids, and neurofibromas.

Progression of the exophthalmos in patients with this endocrine anomaly usually increases steadily with eventual stabilization. We have observed, however, growth spurts as great as five mm. in a two-month period. This contrasts with the intermittent exophthalmos due to hemangiomas and the pulsating exophthalmos typical of a carotid-cavernous sinus fistula.

C. X-ray findings

X-ray films of the orbits are a necessity in any patient with a negative Werner's test. Iliff reported that 42 percent of 200 cases of orbital tumors could be diagnosed by X-ray examination alone.[9] Mucoceles, meningiomas, optic nerve gliomas, and malignancies of the sinus showed the most characteristic changes. As previously stated, in our series radiologic abnormalities were noted in two thirds of the cases of orbital tumors and three of four cases with orbital cellulitis showed X-ray evidence of sinusitis. Orbital films were, however, universally negative in our cases of endocrine exophthalmos.

Summary

1. In a series of 59 patients with unilateral exophthalmos, endocrine dysfunction was established in 21 or 36 percent.

2. Orbital tumors collectively comprised 18 or 31 percent of cases and included 10 different types of neoplasms.

3. Radiologic and physical findings suggested the diagnosis in over 90 percent of orbital tumors and inflammatory lesions.

4. Werner's tri-iodothyronine suppression test was performed in 14 cases presumed to

be endocrine in origin and was positive in each instance. It was negative in four cases with histologically proven orbital tumors. The value of this test is emphasized in evaluating asymmetric proptosis.

5. Clinical features which characterize unilateral endocrine exophthalmos without signs of hyperthyroidism are contrasted with other lesions which may cause unilateral proptosis.

University Hospitals.

References

1. Bullock, L. J., and Reeves, R. J.: Unilateral Exophthalmos. Am. J. Roent., Rad. Ther., & Nuc. Med., **82**:290 (Aug.) 1959.
2. Van Buren, J. M., Poppen, J. L., and Horrax, G.: Unilateral exophthalmos. Brain, **80**:139 (Pt. II) 1957.
3. Drescher, E. P., and Benedict, W. L.: Asymmetric exophthalmos. AMA Arch. Ophth., **44**:109, 1950.
4. O'Brien, C. S., and Leinfelder, P. J.: Unilateral exophthalmos. Am. J. Ophth., **18**:123, 1935.
5. Hamilton, H. E., Schultz, R. O., and DeGowin, E. L.: The endocrine eye lesion in hyperthyroidism. AMA Arch. Int. Med., **105**:675 (May) 1960.
6. Schultz, R. O., Hamilton, H. E., and Braley, A. E.: Ocular changes related to endocrine dysfunction. Am. J. Ophth., **50**:26 (July) 1960.
7. Werner, S. C.: Euthyroid patients with early eye signs of Graves' disease. Am. J. Med., **18**:608, 1955.
8. Schultz, R. O., Van Allen, M. W., and Blodi, F. C.: Endocrine ophthalmoplegia. AMA Arch. Ophth., **63**:217 (Feb.) 1960.
9. Iliff, C. E.: Tumors of the orbit. Tr. Am. Ophth. Soc., **55**:505, 1957.

THE WATER PROVOCATIVE TEST IN GLAUCOMATOUS PATIENTS*

Miles A. Galin, M.D., Futaba Aizawa, M.D., and John M. McLean, M.D.
New York

Various authors[1,2] have described a reduction in the facility of aqueous outflow in the glaucomatous population following the ingestion of one liter of water. This outflow facility reduction has been described to occur even without increase in intraocular pressure. Furthermore, it has been stated that quantitative tonography of this type is helpful in the early diagnosis of open-angle glaucoma.

Previous studies from this laboratory[3] have demonstrated that in the normal population a statistically significant increase in intraocular pressure results following the rapid ingestion of one liter of water. This increase is usually below 6.0 mm. Hg, and is associated with an average reduction in blood osmolality in the range of eight milliosmoles. No statistically significant reduction in outflow facility occurs in these patients, and it has been assumed that an increase in ocular volume occurs to account for the elevation in pressure.

It is the purpose of this communication to evaluate the effect of reduced blood osmolality on the glaucomatous eye, and in turn, to evaluate quantitative tonography in this group.

Materials and Methods

Patients were obtained from the eye clinic of the New York Hospital-Cornell Medical Center. All were past 45 years of age, and had unequivocal open-angle glaucoma, as evidenced by elevated intraocular pressure off medication, accompanied by optic disc and field changes.

The patients were kept in a fasting state following their evening meal the day prior

* From the Department of Surgery (Ophthalmology) of the New York Hospital-Cornell Medical Center. This study was aided in part by grants from the National Society for the Prevention of Blindness and the National Council to Combat Blindness.

TABLE 1*

DATA ON GLAUCOMA PATIENTS STUDIED

	Mo	Mos′	Δ Mos	Po	C	Po′	C′	Δ P
B	289.0	282.0	− 7.0	29.2	0.06	34.4	0.11	+ 5.2
L	295.0	286.0	− 9.0	25.8	0.12	29.2	0.07	+ 3.4
M	291.0	285.0	− 6.0	30.4	0.06	47.8	0.06	+17.4
H	278.0	273.5	− 4.5	29.2	0.08	41.3	0.12	+12.1
H	277.0	271.0	− 6.0	25.8	0.10	33.0	0.07	+ 7.2
N	287.0	283.0	− 4.0	64.0	0.07	81.0	0.07	+17.0
N	287.0	283.0	− 4.0	61.5	0.09	78.4	0.09	+16.9
N	286.0	282.7	− 3.3	69.3	0.02	88.0	0.03	+18.7
N	286.0	282.7	− 3.3	56.9	0.08	81.8	0.05	+24.9
W	289.0	284.0	− 5.0	39.4	0.02	73.2	0.08	+33.4
S	298.0	294.0	− 4.0	25.8	0.08	32.3	0.11	+ 6.5
A	294.0	284.0	−10.0	28.0	0.10	35.1	0.11	+ 7.1
B	283.0	278.0	− 5.0	27.5	0.07	37.3	0.16	+ 9.8
B	283.0	278.0	− 5.0	48.0	0.06	54.7	0.11	+ 6.7
P	285.0	279.0	− 6.0	28.0	0.09	36.5	0.07	+ 8.5
P	285.0	279.0	− 6.0	37.2	0.05	46.0	0.06	+ 8.8
S	288.0	281.0	− 7.0	30.4	0.08	36.5	0.08	+ 6.1
A	285.0	276.0	− 9.0	35.8	0.10	42.6	0.06	+ 6.8
A	285.0	276.0	− 9.0	31.7	0.07	40.2	0.06	+ 8.5
M	288.0	280.0	− 8.0	35.1	0.02	55.8	0.03	+20.7
M	288.0	280.0	− 8.0	35.8	0.02	51.6	0.02	+15.8
P	289.0	286.0	− 3.0	38.7	0.07	46.9	0.05	+ 8.2
L	287.0	286.0	− 1.0	35.8	0.05	43.4	0.10	+ 7.6
L	287.0	286.0	− 1.0	34.4	0.05	41.0	0.06	+ 6.6
B	289.0	284.0	− 5.0	26.9	0.09	35.0	0.11	+ 8.1
R	288.0	280.0	− 8.0	33.0	0.04	35.8	0.05	+ 2.8
R	288.0	280.0	− 8.0	34.4	0.07	38.7	0.06	+ 4.3
L	290.0	282.0	− 8.0	37.7	0.02	45.1	0.02	+ 7.4
B	290.0	281.0	− 9.0	25.8	0.10	30.4	0.05	+ 4.6
S	290.0	286.0	− 4.0	37.2	0.09	38.7	0.06	+ 1.5
S	297.0	293.0	− 4.0	36.5	0.05	41.0	0.06	+ 4.5
S	285.0	282.0	− 3.0	30.4	0.05	38.9	0.11	+ 8.5
E	280.6	270.4	−10.2	29.2	0.08	38.9	0.08	+ 9.7
E	299.9	297.5	− 2.4	28.0	0.06	38.9	0.08	+10.9
E	299.9	297.5	− 2.4	28.0	0.06	37.3	0.08	+ 9.3
E	284.6	277.3	− 7.3	31.8	0.10	37.2	0.05	+ 5.4
E	284.6	277.3	− 7.3	28.0	0.10	33.0	0.03	+ 5.0
C	290.0	289.0	+ 1.0	30.4	0.10	43.9	0.12	+13.5
S	295.0	286.0	− 9.0	28.0	0.10	31.7	0.09	+ 3.7
F	290.2	286.3	− 3.9	30.4	0.05	31.7	0.03	+ 1.3
L	289.0	281.0	− 8.0	29.2	0.15	37.3	0.06	+ 8.1

* Blood osmolality (Mos), intraocular pressure (Po), and outflow facility (C) before and 40 minutes after (Mos′, Po′, C′) the rapid ingestion of one liter of water in 41 glaucomatous patients. The specific changes in milliosmoles and intraocular pressure are listed as ΔMos and ΔP.

to examination. No ocular medication had been used for at least two weeks in the involved eye.

In a group of 41 patients tonography was performed on multiple occasions so that patients became acclimated to the procedure. Applanation and multiple weight recordings with the Mueller electronic tonometer were recorded at all stages of this study, and calculations of ocular rigidity obtained. On the days of testing, blood samples were obtained for subsequent analysis of freezing point depression utilizing a Fiske osmometer. Tonography was then performed, and one liter of water rapidly consumed. Subsequent blood samples were obtained at 15-minute intervals, and tonography again performed approximately 40 minutes following water consumption.

In 23 members of this glaucomatous population a similar study was carried out using isosmotic saline as the provocative agent.

Outflow facility was calculated utilizing Moses' and Becker's tables based on Friedenwald's data.[4] When any change of ocular rigidity was noted the data were recalculated

to be comparable to those of average rigidity. Flow in cubic milliliters per minute was calculated by the equation $F = C(Po\text{-}Pv)$. No direct measurements of Pv (episcleral venous pressure) were obtained, and this value was assumed to be 11.7 mm.

Results

Table 1 lists the pertinent data in this group. It should be noted that a statistically significant reduction in blood osmolality occurs, as well as a highly significant increment in intraocular pressure. Ocular volume is significantly increased, and no statistically significant change occurs in outflow facility. Tonographically interpreted this data would indicate an increase solely in aqueous flow.

Table 2 compares the response to water and isosmotic saline in 23 patients included in Table 1. Though some patients had moderate changes in intraocular pressure, the over-all change is not statistically significant and is distinctly different from these patients' response to water. The changes in blood osmolality following saline are similar to data previously published and will not be repeated here.

Discussion

There is good evidence that increments in intraocular pressure following water drinking are initiated by changes in blood osmolality. In the normal population a statistically significant increase in intraocular pressure occurs following the rapid ingestion of one liter of water. This is unaccompanied by a statistically significant change in outflow facility, but is associated with a statistically significant reduction in blood osmolality. In animals, large reductions in blood osmolality result in large increments of intraocular pressure, while smaller osmole changes yield smaller intraocular pressure changes. Isosmotic saline in amounts equal to the volume of ingested water cause little change in intraocular pressure.[5] Similar data have been obtained in humans.[6]

The results of this study appear to be an extension of the data obtained in normal humans and animals. In patients with ele-

TABLE 2*

Comparison of response to water and isosmotic saline

	P_o	C	P′	C′	ΔP_s	ΔP_w
1	30.4	0.10	30.4	0.10	0.0	+ 6.1
2	25.3	0.11	24.3	0.08	− 1.0	+ 6.9
3	29.8	0.10	26.4	0.09	− 3.4	+ 8.5
4	28.0	0.02	40.5	0.09	+12.5	+15.9
5	48.7	0.03	56.9	0.07	+ 8.2	+ 8.2
6	33.0		28.0		− 5.0	+ 3.5
7	42.6	0.02	49.7		+ 7.1	+ 7.6
8	42.6	0.02	46.9	0.03	+ 4.3	+ 6.6
9	28.0	0.05	29.8	0.11	+ 1.8	+ 8.1
10	31.7		30.4		− 1.3	+ 2.8
11	35.8	0.10	35.8	0.06	0.0	+ 4.3
12	27.5		34.4		+ 6.9	+ 7.4
13	41.8	0.10	43.4	0.07	+ 1.6	+ 6.7
14	34.4	0.12	20.6	0.17	−13.8	+ 7.0
15	25.8	0.12	21.0	0.19	− 4.8	+ 2.1
16	25.8	0.07	25.8	0.09	0.0	+ 4.6
17	52.6	0.02	51.6	0.02	− 1.0	+14.9
18	61.5	0.04	64.0	0.02	+ 2.5	+18.7
19	59.1	0.05	59.1	0.03	0.0	+24.9
20	50.6	0.02	59.1	0.02	+ 8.5	+33.8
21	25.8	0.09	24.8	0.06	− 1.0	+ 9.1
22	25.3	0.16	20.6	0.18	− 4.7	+ 6.5
23	50.6		59.1		+ 8.5	+15.3

* Intraocular pressure (Po) and outflow facility (Co) in a group of glaucomatous patients before and 40 minutes after (Po′, C′) the rapid ingestion of one liter of isosmotic saline. The change in pressure following saline (ΔPs) is compared to the change in pressure following water (ΔPw).

vated intraocular pressure significant reductions in blood osmolality lead to large changes in intraocular pressure with no significant change in outflow facility. This glaucomatous population does not vary from normal with respect to osmole reduction following water ingestion, and there is no reason to believe that they handle water differently than normals. A comparison of the effects of water and isosmotic saline in this group clearly indicates that the effects may be largely explained on the basis of osmotic gradients. One need not consider primary changes in outflow facility to explain the intraocular pressure changes.

Other investigators have also been unable to demonstrate significant reproducible reduction in outflow facility following water ingestion in glaucomatous patients.[7,8] It is of interest in this regard that in a recent study of the families of glaucomatous patients,[9] six patients were found to have intraocular pressures in the glaucomatous range, and four of these patients were given the water drinking test. Three eyes responded with a reduction in outflow facility, two eyes were unchanged, and three were improved. This distribution is in keeping with data found in normals, as well as the glaucomatous subjects reported here.

Careful attention in this study was paid to ocular rigidity. At the outset it is well known that inconsistent rigidity measurements are frequently obtained. It is also not uncommon to find different slopes to the rigidity curve depending on which pair of weights is utilized. Consequently, when rigidity measurements appeared altered by water drinking, the data were recalculated to be comparable to the prewater rigidity measurement. However, in no cases of this group could we obtain a consistent, reproducible change in rigidity following water. This observation is similar to results reported in normals[3] as well as glaucoma patients [10] following water ingestion, and differs from Becker and Gay's reports.[11]

The data in this study indicate that a glaucomatous patient experiences a reduction in blood osmolality following the rapid ingestion of one liter of water. The already hypertensive eye responds with large increments of pressure to small changes in ocular volume, particularly if the outflow facility is low and it is difficult to handle the increased ocular volume. The pressure increase is not necessarily accompanied by a change in outflow facility.

Summary

Following the rapid ingestion of one liter of water, a glaucomatous patient will have a reduction in blood osmolality in the order of eight milliosmoles, associated with an increase in intraocular pressure. This sequence does not occur following the ingestion of one liter of saline. In neither case is there a significant reproducible change in outflow facility or ocular rigidity.

525 East 68th Street (21).

References

1. Becker, B., and Christiensen, R. E.: Water drinking and tonography in the diagnosis of glaucoma. AMA Arch. Ophth., **56**:321, 1956.

2. Roberts, W.: Tonographic criteria in early glaucoma: Clinical tonography as an aid to the diagnosis and management of early glaucoma. Am. J. Ophth., **48**:31 (Nov. Pt. I) 1959.

3. Galin, M. A., Aizawa, F., and McLean, J. M.: Evaluation of the water provocative test. Am. J. Ophth., **51**:451, 1961.

4. Moses, R. A., and Becker, B.: Clinical tonography: The scleral rigidity correction. Am. J. Ophth., **45**:196, 1958.

5. Galin, M. A., Aizawa, F., and Baras, I.: Studies on the mechanism of the water drinking test. Am. J. Ophth., in press.

6. Galin, M. A., Aizawa, F., and McLean, J. M.: The Osmotic effects of the water provocative test. In preparation.

7. de Roetth, A., Jr.: Effect of changes in osmotic pressure of blood in aqueous humor dynamics. AMA Arch. Ophth., **52**:571, 1954.

8. Scheie, H. G., Spencer, R. W., and Helmich, E. D.: Tonography in the clinical management of glaucoma. AMA Arch. Ophth., **56**:797, 1956.
9. Becker, B., Kolper, A. E., and Roth, F. D.: Glaucoma family study. Am. J. Ophth., **50**:557, 1960.
10. Stepanik, J.: Das Verhalten der Skleralrigidität während des Wassertrinkversuches. Ophthalmologica, **136**:174, 1958.
11. Becker, B., and Gay, A.: Applanation tonometry in the diagnosis and treatment of glaucoma. AMA Arch. Ophth., **62**:211, 1959.

FIXATION ANOMALIES IN AMBLYOPIA EX ANOPSIA

MARTIN J. URIST, M.D.
South Haven, Michigan

Duke-Elder[1] defines fixation as, "when a light stimulus falls upon a peripheral part of the retina and is appreciated by consciousness the eyes are reflexly moved in such a way that the image falls on the fovea."

The simplest and most commonly used method for observing fixation is to cover one eye and have the subject look at a light with the uncovered eye. One then notes the ability to fix the light and the position of the corneal reflex in relation to the anatomic center of the cornea. This method, however, does not permit one to determine normal foveal fixation. Fixation may be a few degrees parafoveal yet the corneal reflex will appear centric. Also, in cases in which the fovea has become displaced, developmentally or pathologically, fixation may be foveal, yet the corneal reflex will be grossly displaced. These are eyes with large angle kappas.

In eyes with a large positive angle kappa the corneal reflex is seen nasally because the fovea is in a more temporal position than normal and the eye appears exotropic. When a large negative angle kappa is present, the corneal reflex is seen temporally because the fovea is displaced in a more nasal position and the eye appears esotropic.

In order to diagnose fixation anomalies accurately, it is important to look into the fundus and note whether the fovea is the actual fixing point. If foveal fixation is present, the position of the fovea relative to the disc, both horizontally and vertically, must be compared in the two eyes. It must also be compared with the normal to rule out unilateral and bilateral abnormal angle kappas.

In cases of strabismus with amblyopia ex anopsia, fixation anomalies are frequently seen. It is of importance that these be recognized early so that treatment of amblyopia can be started. In young children the corneal reflex method is the most practical one to use. Some of the common types of fixation anomalies as observed by this method will be discussed.

1. CENTRIC MACULAR FIXATION (PARAFOVEAL)

These cases have centric fixation as determined by the corneal reflex method. However, in co-operative cases in which it can be determined by funduscopy, fixation will be found to be away from the fovea. This is done by having the patient fix on a narrow slit of light which has been projected on to the retina with the ophthalmoscope or on a small figure, as with the Visuscope, and observing the position of the slit or figure relative to the foveal reflex. It will be seen that the light slit or figure does not pass through the foveal reflex but to one side of it, even as far out as the edge of the macula. The vision in the amblyopic eye in this group is usually better than 20/200.

Cases of fixation disparity may be included in this group of parafoveal fixation. In binocular vision they have parafoveal fixation in one eye (enlarged Panum's area); in monocular vision, however, when the nor-

mal eye is occluded, the uncovered eye moves toward the fovea to take up fixation. This shift in fixation may give the impression of a true squint with the alternate cover test.

2. Uncertain fixation

In these cases the amblyopia is usually more severe than with centric macular fixation. Fixation varies from centric to five to 10 degrees away from the macula. With attention and effort by the subject, centric fixation can be maintained for a short interval. Proper occlusion of the good eye is usually successful in bringing about a return of vision and fixation.

3. Wandering fixation

These are cases of profound amblyopia, usually below 5/200. The fixation reflex appears to be present but not constant in any one position on the retina. The eye wanders about and the corneal reflex varies with the variability of the eye movements. Proper occlusion of the good eye can bring about return of vision and centric fixation.

4. Eccentric fixation

This most interesting type of fixation anomaly is the principal subject of this study. The characteristic and very striking feature of these cases of strabismus is complete absence of any recovery movement when the fixing eye is occluded. Fixation remains at an eccentric area, away from the macula, usually at the angle of squint. The cross-cover test can be done any number of times and yet eccentric fixation is so marked that absolutely no movement is seen, not even a phoria movement. Because of this, the theory was advanced that the normal macula had become suppressed and a new area or functional macula at the angle of squint had developed. This new functional macula was considered to have become the dominant area for fixation. Because of the possibility of consolidating the new functional macular area some authorities[2,3] have advised against occluding the good eye in treating the amblyopia.

A study of a group of cases of apparent eccentric fixation in which there was no movement with the cross-cover test revealed that the clinical course was not consistent with the concept that a new functional macula had developed. The findings in these cases were such that, instead of a new area on the retina developing dominance, it appeared that the whole retina had a diminished power of fixation. In fact, in most cases, it was found that the whole retina had lost the ability to fix a light. The term "afixation," meaning no fixation, could better describe such findings than eccentric fixation and will be used throughout this paper. The following cases will illustrate this point.

Case reports

Case 1

A seven-year-old boy (123) was brought to the infirmary in 1947 with a history of the right eye being crossed since two years of age. With atropine cycloplegia, refraction was: O.D., +2.5D. sph. = 1/200 eccentric fixation at 20 degrees of esotropia; O.S., +1.25D. sph. = 20/20.

There were 20 degrees of right esotropia with and without glasses for distance and near (fig. 1). The near-point of convergence was 30 mm. No movement was found with the cover test. No after-image could be elicited in the right eye, although a good after-image was found in the left eye. Complete occlusion of the left eye was advised to attempt to bring the vision up in the right eye but no co-operation was obtained from the child or parents, who wanted cosmetic surgery.

Surgery, on August 6, 1947, consisted of a five-mm. recession of the right medial rectus muscle and an eight-mm. resection of the right lateral rectus muscle. Following this, the eyes became cosmetically straight for distance and near, with and without glasses (fig. 1-e, f, g). Fixation in the right eye appeared to be centric now. Vision still was 1/200 with no movement with the cover test. The near-point of convergence was still 30 mm.

For about six months the eyes remained cosmetically straight; then they began to diverge. Examination one year after surgery revealed 20 degrees of right exotropia for distance and near with and without glasses (fig. 1-i, j). Fixation was eccentric at 20 degrees of divergence and again there was no movement with the cover test. Vision was still 1/200 in the right eye.

Comment. Before surgery eccentric fixation was at 20 degrees of esotropia in the right eye. The fixation appeared to be so well established that no movement, not even a slight phoria movement, could be elicited with the cross-cover test. From this finding the accepted concept that a new eccentric

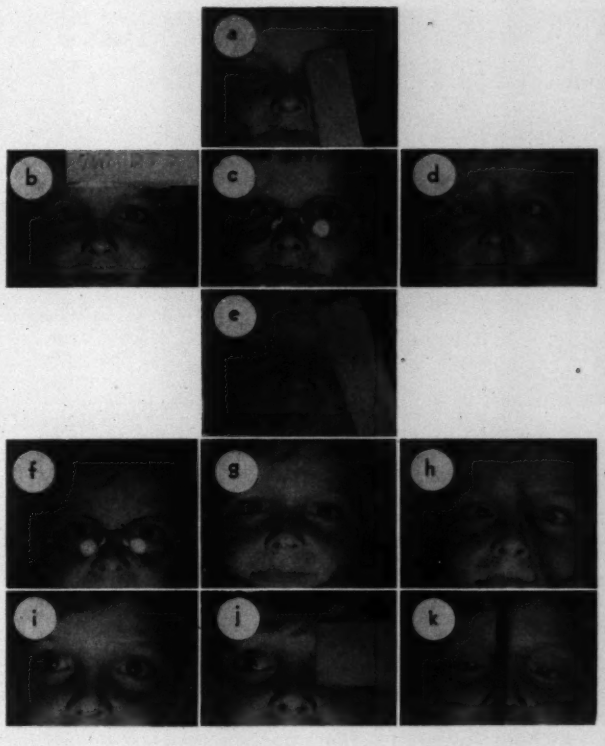


Fig. 1 (Urist). *Case 1*

Before surgery

(a) Eccentric fixation of the right eye at 20 degrees of esotropia. Vision in the right eye was 1/200.

(b) Twenty degrees of right esotropia without glasses for distance and near. Vision in the left eye, 20/20.

(c) Twenty degrees of right esotropia with glasses for distance (and near).

(d) Near-point of convergence, 25 mm.

Four months after operation

(e) Centric fixation of the right eye. Vision in right eye, 1/200.

(f) Straight eyes with glasses for distance (and near).

(g) Straight eyes without glasses for distance (and near).

(h) Near-point of convergence, 25 mm.

One year after operation

(i) Twenty degrees of right exotropia for distance and near without glasses. Vision in the left eye, 20/20.

(j) Eccentric fixation of the right eye at 20 degrees of divergence. Vision in the right eye, 1/200.

(k) Near-point of convergence, 40 mm.

area of the right eye had developed fixation dominance certainly appeared reasonable. Immediately after surgery on the right eye the eyes were straight and fixation was centric in each eye. Again no movement was found with the cover test. This was difficult to explain because if an eccentric functional macula had been present one would expect some time to elapse before it would lose its dominance. One would expect some movement for it to take up fixation after surgery (see Case 7). However, it was reasoned that the true macula had suddenly taken up fixation in preference to the eccentric area. How this was possible with the vision still 1/200 remained unclear.

After a time the eyes diverged and again no movement with the cover test occurred at the angle of exotropia. This finding, together with the previous findings, made the whole concept of a fixed eccentric functional macula unapplicable to this case.

An alternate explanation could be derived from the concept that the retinal suppression had affected the fixation reflex to such an extent that it was lost and that the eye was under no compulsion to change its position when the fellow eye was covered. In other words, no fixation in any sense of the word was present at the angle of squint. Evidence for this was found when optokinetic nystagmus was tested. Using a drum with black and white stripes large enough to be easily seen by the amblyopic eye, no nystagmus could be elicited on rotation of the drum while the fellow eye showed typical optokinetic nystagmus. The suppression of vision and fixation in the squinting eye was associated with suppression of the ability to perceive an after-image with the Bielschowsky test.

CASE 2

A 20-year-old man (2-154) was first seen at the infirmary on September 29, 1949. He gave a history of having had very crossed eyes when a young child. The eyes had straightened but the left eye still crossed at times for near.

With atropine cycloplegia refraction was: O.D., +1.5D. sph. = 20/20; O.S., +4.0D. sph. ⌒ +1.0D. cyl. ax. 90° = 5/200.

Examination revealed the eyes to be straight for distance and near, that is, the left corneal reflex was centric and no movement could be found with the cover test (fig. 2-a, b). At times, especially for near, there was 15 degrees of left esotropia (fig. 2-c, d) and again no recovery movement could be obtained with the cover test.

Comment. This was one of the most interesting cases in the series of fixation anomalies. Whether the eyes appeared straight or 15 degrees convergent with the corneal reflex test, there was no movement

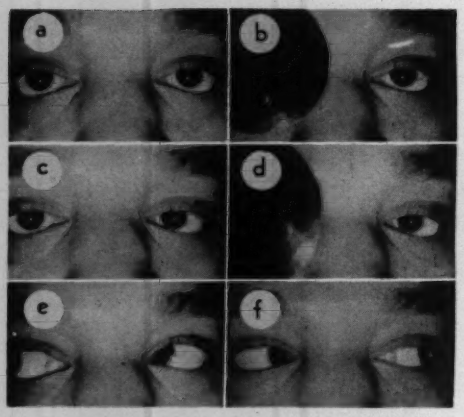


Fig. 2 (Urist). *Case 2.* (a) Eyes straight for distance. Vision in the right eye, 20/20; in the left, 5/200. (b) Centric fixation of the left eye. Vision in the left eye 5/200, no movement with the cover test. (c) Fifteen degrees of left esotropia for near. (d) Eccentric fixation of the left eye for near at 15 degrees of convergence. No movement with the cover test. (e) Elevation of the left eye in adduction. (f) Eyes level on gaze to the left; good abduction present.

with the cover test. If one believed in the development of a secondary fixation area, this finding could be explained as follows:

Two areas of fixation had developed, one macular or centric operating when the eyes were straight, the other at 15 degrees of esotropia operating when the eyes were crossed. This might be compared with two areas of retinal correspondence in the same eye, one normal and the other abnormal.

There were findings, however, which did not support this explanation. If centric fixation and possible macular function were present the vision should be better when the macular area fixed than when the eccentric area fixed. This was not the case as the vision was 5/200 in both positions. With two areas of fixation in the same eye, some form of monocular diplopia should be obtainable which was not the case. If a peripheral part of the retina did assume fixation, instead of the macula there should at some time have been a movement of the eye toward that point (see Case 7). This was never found.

If a fixation mechanism of any kind were present, one would expect some small phoria movement. In normal cases with the best possible foveal fixation and stereopsis it is rare not to find a small phoria movement. In this case absolutely no movement in either position, centric or eccentric, was found with the cross-cover test. Here again an after-image was not perceived by the amblyopic eye and no optokinetic nystagmus could be elicited. These clinical findings indicated that severe retinal suppression was present and that there was complete loss of fixation.

CASE 3

A nine-year-old boy was brought to the infirmary on May 31, 1950, with a history of the right eye having been crossed since birth. Refraction with atropine cycloplegia was: O.D., +2.25D. sph. = 5/200; O.S., +1.75D. sph. = 20/30.

Examination (fig. 3) revealed a right esotropia that varied from 20 degrees with glasses to 25 degrees without glasses. Looking up the esotropia was 25 degrees while looking down it was 15 degrees. No matter what the angle of squint was, fixation in the left eye was constant at the respective angle of squint and no tropia movement was seen with the cross-cover test.

Comment. If one adhered to the concept of eccentric fixation, how would the findings in this case be explained? Since the eccentric fixation area varied with the many angles of squint in the different position of gaze one might postulate that a new eccentric functional macula had developed for each of them. This would require a concept of multiple functional eccentric fixation areas developing on the retina. Such a concept seems unlikely since the squint was so variable. On the other hand, the concept of loss of fixation did fit the clinical findings well. No matter what the anatomic position of the eye the corneal reflex remained there. This case also had all the findings of deep retinal suppression in the amblyopic eye, namely, 5/200 vision, inability to perceive an after-image, no optokinetic nystagmus and, in addition, an atypical pupillary reaction that is not uncommonly seen in this type of case, namely, dilation of the pupil in the amblyopic eye to a light when the good eye was occluded (fig. 3-j, k, l).

CASE 4

A seven-year-old girl (267) was brought to the infirmary in June, 1949, with a history of the right eye turning in since the age of three years. With atropine cycloplegia refraction was: O.D., +2.75D. sph. $\bigcirc$ +0.5D. cyl. ax. 105° = 2/200; O.S., +2.75D. sph. $\bigcirc$ +0.75D. cyl. ax. 90° = 20/20.

Examination (fig. 4) revealed 20 degrees of right esotropia. There was "afixation" of the right eye at 20 degrees of esotropia, as well as limitation of the right eye in abduction with increased movement in adduction when compared to the left eye. Total occlusion of the left eye was carried out for six months. The vision in the right eye improved to 20/30 and fixation was regained. When the patch was removed from the left eye, it was found that a left esotropia of 20 degrees was present and fixation was lost. "Afixation" of the left eye had developed since there was no movement with the cross cover test. Now the left eye showed limitation in abduction and increased movement in adduction when compared to the right eye. The vision in the left eye was remarkable in that it was 20/30. The mother was instructed to occlude the straight eye for half a day and when watching television. This was done and after one

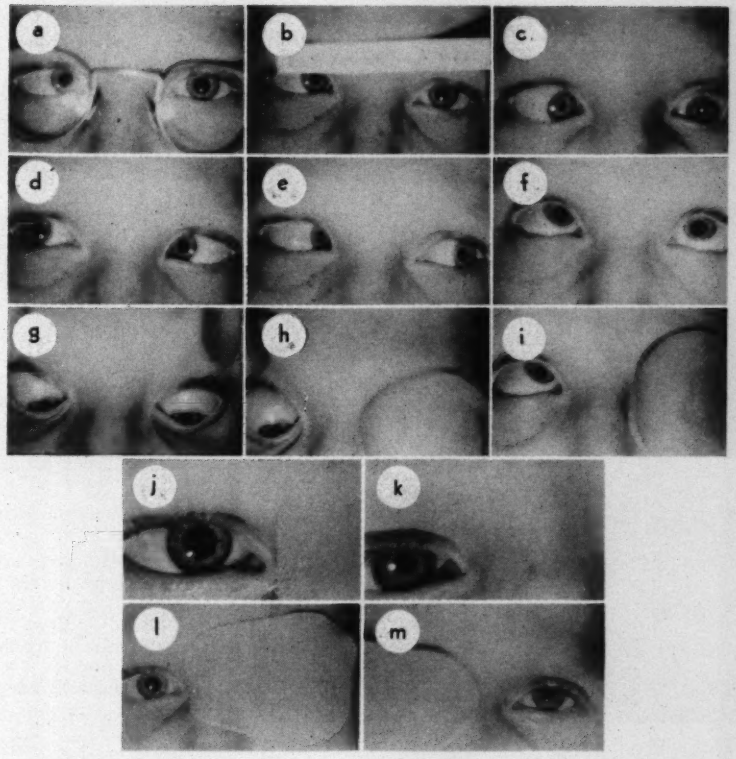


Fig. 3 (Urist). *Case 3.* (a) Twenty degrees of left esotropia for distance with glasses—pupils equal. (b) Twenty-five degrees of left esotropia for distance without glasses—pupils equal. (c) Thirty-five degrees of left esotropia for near without glasses—pupils equal. (d) and (e) Limitation of the right eye in abduction with increased adduction compared with the left eye. (f) Twenty-five degrees of right esotropia looking up. (g) Fifteen degrees of right esotropia looking down. (h) Afixation of the right eye at 15 degrees of esotropia looking down. (i) Afixation of the right eye at 25 degrees of esotropia looking up. (j) Afixation of the right eye at 20 degrees of esotropia. Note the large pupil when the left eye was occluded. (k) Afixation of the right eye at 20 degrees of esotropia. Note the small pupil when the left eye was not occluded. (l) and (m) With equal illumination the right pupil is larger compared to the size of the left pupil.

week, when the patient was seen again, she had regained fixation in the left eye and it was centric in each eye. The vision at this time was 20/20 in each eye and no limitation in motion was seen. "Afixation" had completely disappeared in that good recovery movement was found with the cross-cover test. This patient had surgery and an excellent postoperative result.

Comment. After six months of complete occlusion, "afixation" developed in the occluded eye. This could hardly have been due to a new functional macula developing through usage. Occlusion had caused a suppression of the fixation reflex of the retina. It also had produced a functional limitation of movement in the eye. The finding of 20/30 vision in an eye with "afixation" may be explained by the fact that visual acuity seldom becomes suppressed after the age of seven years, but it was possible to suppress the fixation reflex by occlusion though it returned very quickly when the eye was uncovered. When seen one week later, fixation was centric and the functional limitation in abduction had disappeared. It may be that the functional limitation in abduction had some influence on the facility for fixation movements.

Case 5

A six-year-old girl (4-118) was brought to the infirmary in June, 1954, with a history of the left eye turning in since birth. She was a congenital

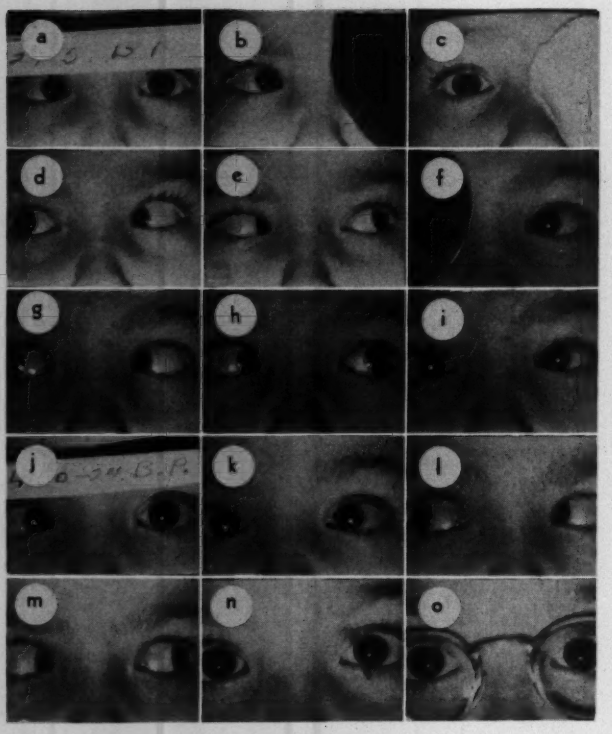


Fig. 4 (Urist). *Case 4.*

Before Occlusion

(a) Twenty degrees of right esotropia.

(b) Afixation of the right eye at 20 degrees of esotropia.

(d) and (e) Limitation of the right eye in abduction with increased movement in adduction when compared to the left eye.

After complete occlusion of the left eye for six months

(c) Centric fixation of the right eye.

(f) Afixation of the left eye at 20 degrees of esotropia.

(g) and (h) Limitation now of the left eye in abduction with increased adduction as compared to the right eye.

(i) Twenty degrees of left esotropia.

After vision was equalized with partial occlusion

(j) Twenty degrees of right esotropia and centric fixation of the left eye.

(k) Twenty degrees of left esotropia and centric fixation of the right eye.

(l) and (m) Both eyes move out well.

After surgery

(n) Five degrees of right esotropia without glasses.

(o) Straight with glasses.

cerebral spastic. With atropine cycloplegia, refraction was: O.D., +3.0D. sph. = 20/40; O.S., +2.0D. sph. = 5/200.

Examination (fig. 5) revealed 25 degrees of left esotropia with and without glasses and "afixation" in the left eye. No optokinetic nystagmus could be elicited and no after-image could be perceived by the left eye. The left pupil markedly dilated to a light when the right eye was covered. Complete constant occlusion of the right eye was instituted. After one year of constant occlusion, the vision in the left eye had improved to 15/200 and the position of the corneal reflex had become variable. It could be at 20 degrees of esotropia, 10 degrees of esotropia or centric. Complete patching was continued. Three years later vision in the left eye was 20/100. At this time the corneal reflex was in a position of 15 degrees of divergence when the patient looked at a light. When the patch over the right eye was removed, the corneal reflex in the left eye still corresponded to 15 degrees of divergence while that of the right eye corresponded to 45 degrees of convergence with "afixation." After a short time, fixation returned and became centric in the right eye with remaining "afixation" of the left eye at 25 degrees of esotropia. Patching was discontinued and in August, 1959, a five-mm. recession of the left medial rectus muscle and an eight-mm. resection of the left lateral rectus muscle were done. Postoperative examination on November 5, 1959 (fig. 5-i, j) revealed the eyes to be straight with glasses. Vision in the left eye at that time was 10/200 with centric "afixation" present.

Comment. In this patient the effect of occlusion on a case of marked apparent eccentric fixation was seen. Occlusion of the good eye did not make the area of eccentric fixation at 25 degrees more fixed but changed it. The corneal reflex moved toward the macula from the original 25 degrees of esotropia to 15 degrees to centric. However, in this case, although the vision improved to better than 20/200, when the reflex was centric, the macular suppression was not relieved and the "afixation" persisted. The corneal reflex continued to move to a divergent position of 15 degrees. In most cases of "afixation," when the corneal reflex has moved to the centric position the vision improves rapidly and fixation is recovered and remains centric. It is possible that in this case there

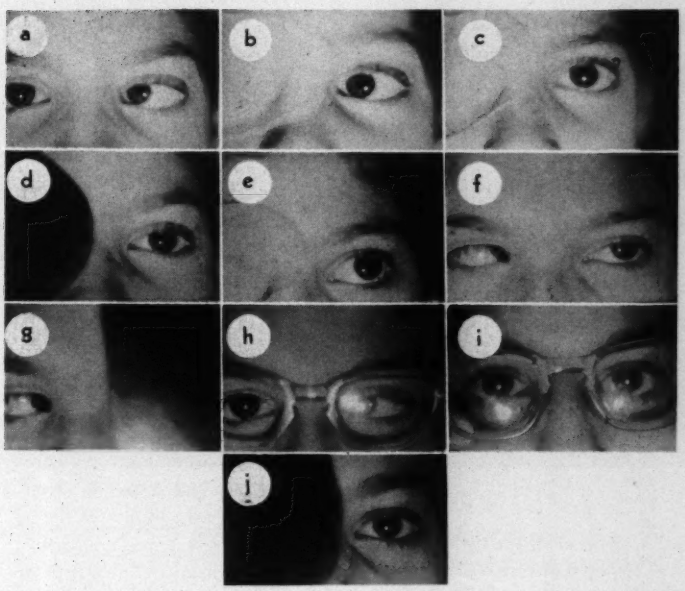


Fig. 5 (Urist). *Case 5.* (a) Twenty-five degrees of left esotropia. (b) Afixation at 25 degrees of left esotropia.

After occlusion of the right eye for one year

(c) Afixation at 10 degrees of left esotropia.
(d) Centric afixation.

Three years later

(e) Afixation at 15 degrees of left exotropia.

When patch was removed from the right eye

(f) Afixation at 15 degrees of left exotropia; also at 45 degrees of right esotropia.
(g) Afixation at 45 degrees of right esotropia.

One hour later

(h) Afixation of the left eye at 25 degrees of esotropia.

Three months postoperative

(i) Straight with glasses.
(j) Centric afixation of the left eye.

was some macular or cerebral damage since she was a spastic and the vision could not be improved beyond 20/100. The finding of a change in the angle of squint from a convergent to a divergent position with patching of the good eye may be a bad prognostic sign for visual improvement.

CASE 6

A seven-year-old girl (4-227) was brought to the infirmary on June 4, 1956, with a history of the left eye being crossed since birth. With atropine cycloplegia refraction was: O.D., +2.25D. sph. = 20/20; O.S., +4.5D. sph. = counting fingers at two feet.

Examination (fig. 6) revealed 20 degrees of left esotropia with "afixation" of the left eye. Total 24-hour-a-day occlusion of the right eye was instituted, and, after six months of total occlusion the vision in the left eye was 10/200. With the right eye occluded, a change in the position of the corneal reflex in the left eye could be seen. It varied from 10 degrees of esotropia to centric to 15 degrees of divergence. When the patch was removed from the right eye, the corneal reflex was seen to be at 15 degrees of esotropia in the right eye and 10 degrees of esotropia in the left eye. "Afixation" was present since no movement was found by the cover test. After a few minutes, fixation was recovered and became centric in the right eye but, in the left eye, the corneal reflex was at 20 degrees of esotropia with "afixation." The patient refused to continue patching. Final vision was 20/20 in the right eye and 15/200 in the left.

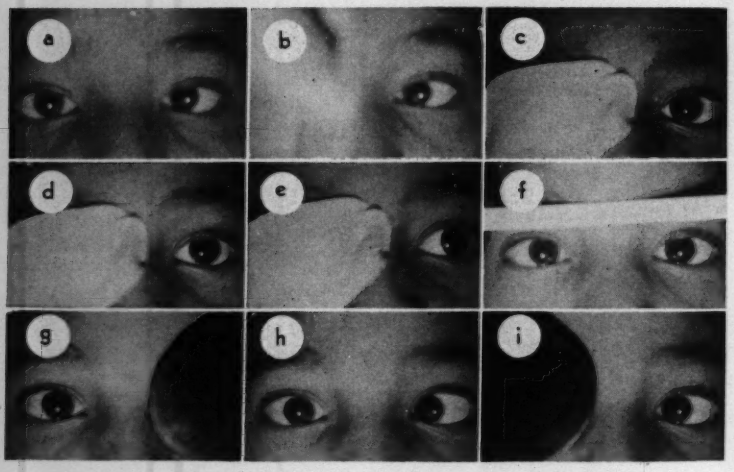


Fig. 6 (Urist). *Case 6.* (a) Twenty degrees of left esotropia. (b) Afixation at 20 degrees of left esotropia.

After total occlusion of the right eye for six months

(c) Afixation at 10 degrees of left esotropia.
(d) Centric afixation.
(e) Afixation at 15 degrees of left exotropia.

Immediately after patch was removed from the right eye

(f) Afixation of the right eye at 15 degrees of esotropia, of the left eye at 10 degrees of esotropia
(g) Afixation of the right eye at 15 degrees of esotropia.

One-half hour after patch was removed from the right eye

(h) Centric fixation of the right eye, 20 degrees of left esotropia.
(i) Afixation at 20 degrees of left esotropia.

Comment. Occlusion of the fixing eye in this case certainly did not consolidate the apparent area of eccentric fixation. In fact, it did the opposite. It changed the position of the eye with "afixation." When the patch was first removed, there was temporary loss of fixation of the occluded eye. As in Case 5, this demonstrated that "afixation" was caused by occlusion and not by the continued use of a noncorresponding area. In this case also the corneal reflex moved to a divergent position which appeared to be a bad prognostic sign for the return of macular vision and fixation.

The next case to be reported was the only one seen in our clinic with findings consistent with the concept that a new functional eccentric macula had developed to take up fixation.

CASE 7

A 15-year-old boy (4-276) came to the infirmary on August 6, 1957, with a history of the left eye having turned in since the age of three years. With atropine cycloplegia, refraction was: O.D., +2.0D. sph. ⊃ +0.5D. cyl. ax. 90° = 20/15; O.S., +2.0D. sph. = 7/200 vision.

Examination revealed 15 degrees of left esotropia with glasses and 30 degrees of left esotropia without glasses. In the left eye eccentric fixation was noted at 15 degrees of esotropia. On December 5, 1957, a five-mm. recession of the left medial rectus muscle and a seven-mm. resection of the left lateral rectus muscle were done.

Postoperative examination on June 12, 1958 (fig. 7) revealed that with the Hirschberg corneal reflex test the eyes were straight with glasses and about 10 degrees convergent without. When the right eye was covered, the left eye moved in to fix at about 15 degrees of esotropia with and without glasses. Vision was still 7/200 in the left eye. Cover measurements were:

c/c/ XT 30Δ, XT′ 30Δ
s/c/ XT 25Δ, XT′ 35Δ

Comment. After surgery, in contrast to the cases of afixation presented, there was movement of the amblyopic eye to take up fixation when the right eye was covered. The left eye moved from a centric position to the old preoperative area of 15 degrees

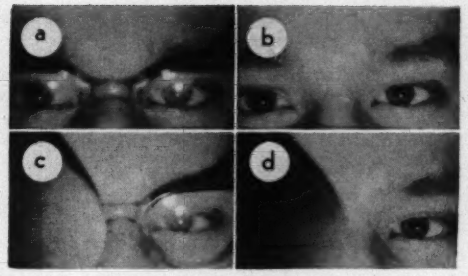


Fig. 7 (Urist). *Case 7*

Six months after surgery

(a) Straight with glasses.
(b) Ten degrees of left esotropia without glasses.
(c) Eccentric fixation at 15 degrees of left esotropia with glasses.
(d) Eccentric fixation at 15 degrees of left esotropia without glasses.

of esotropia. This gave the unusual finding of paradoxical exotropia, that is, base-in cover measurements in the presence of esotropia. In addition, when the left eye fixed the small beam of the ophthalmoscope light and the fundus was examined, fixation was always in the same area of the retina, nasal to the disc. From these findings it certainly was plausible to assume that a new area of the retina, nasal to the disc, had achieved dominance for fixation.

Another confirmatory finding for this was the normal optokinetic nystagmus present in that eye. However, other signs of retinal suppression were present, such as, the 7/200 vision, the atypical pupillary reaction in dilating to a light and the inability to perceive an after-image. In this case occlusion of the good eye to bring up vision would appear to be contraindicated since it could consolidate the eccentrically fixing area.

Discussion

The following are the important findings in cases of "afixation":

1. *Amblyopia.* The vision is usually less than 20/200.

2. *Absent fixation.* No movement can be demonstrated with the cover test. The fixation reflex or movement toward a spot on the retina has been lost. The angle of squint can only be measured on the perimeter or with the corneal reflex test. In the cases presented, it was seen that no matter where the eyes were placed, whether the changes in the angle of squint came about naturally or following surgery, no movement took place with the cover test. No new point on the retina took up fixation. With this concept in mind, occlusion of the good eye certainly could not consolidate the area of fixation as promulgated in the literature.[2,3] The results of occlusion of the good eye in my hands on the whole have been good.[4]

3. *Absence of an after-image.* In a series of 45 cases that were tested with the Bielschowsky light, 43 claimed they could not see an after-image in the amblyopic eye but saw one well in the good eye. In two cases the patients thought they saw the after-image in the amblyopic eye but this was not confirmed when positive and negative after-images were used to check the responses. Guibor[5] reported that his patient saw the after-image in the amblyopic eye. Since my patients could not obtain an after-image in the eye with "afixation," it was not possible to test the retinal correspondence with this test.

4. *Absent or diminished optokinetic nystagmus.* For elicitation of this reflex I used a rotating drum having stripes large enough to be easily seen by the amblyopic eye. The optokinetic nystagmus response in the amblyopic eye was absent in most patients and poor compared to the good eye in the others. In cases of "afixation" that he tested, Folk[6] found no optokinetic nystagmus in the amblyopic eye. In contrast to these cases, five cases of Kuhnt-Junius macular disease with vision of less than 5/200 were tested with the same drum. All of these had excellent optokinetic nystagmus.

5. *Central scotomas.* When fields were taken in 10 cases of "afixation" in which good co-operation was obtained, a large central scotoma which included the blindspot was found. The finding of Chavasse[7] of a macular scotoma and a new area of fixation with an otherwise good field could not be confirmed.

6. *Unusual pupillary phenomenon.* In many cases the pupil of the amblyopic eye was more dilated to the same stimulus than the pupil of the good eye. This has been brought out by Harms.[8]

7. *Limitation in abduction* and increased

movement of the eye with "afixation" in adduction were common findings in these cases. Apparent vertical limitation of movement may be seen. These limitations are usually functional and will improve when the vision and fixation improve.

8. *Loss of entopic phenomena.* In a few cases, the auto-entopic test was done and most of the patients could not see their retinal blood vessels. One patient could see the area of the disc and a black area in the central region.

9. *Proprioceptive phenomena.* All of the 10 patients who were tested did not consistently past-point or past-walk when the good eye was covered. Guibor[5] found that his patients past-pointed and past-walked.

10. "*Afixation*" can be produced in a normal eye after prolonged occlusion and is usually accompanied by a marked loss of vision. In one case it occurred with 20/30 vision. The vision and fixation, as a rule, returned very quickly when the patch was removed.

Summary

Fixation anomalies that occurred with strabismus were usually accompanied by other findings of retinal suppression such as amblyopia ex anopsia, loss of ability to see an after-image, loss of optokinetic nystagmus and atypical pupillary reactions.

Types of fixation anomalies commonly seen with the corneal reflex test were (1) centric macular fixation (parafoveal), (2) uncertain fixation, (3) wandering fixation and (4) loss of fixation ("afixation"). The new term, "afixation," was used to describe those cases that had apparent marked eccentric fixation at the angle of squint in which there was no movement with the alternate cover test. The term was used because we found that these cases probably had complete retinal suppression of fixation and not fixation by a newly developed eccentric area. In these cases occlusion of the good eye was indicated for the return of vision and fixation and gave good results.

The rarest fixation anomaly, of which only one case was seen in our clinic, was that of true eccentric fixation. In this case, in contrast to cases of "afixation," there was movement with the cross-cover test in order for an eccentric retinal area, nasal to the disc, to take up fixation. In this case occlusion of the good eye would be contraindicated as it might be expected to consolidate the eccentric area of fixation.

432½ Phoenix Street.

References

1. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, Mosby, v. 1, 1939, p. 621.
2. Swan, K. C.: Sensory physiology of binocular vision. In Strabismus Ophthalmic Symposium (edited by Allen). St. Louis, Mosby, 1950, p. 124.
3. Daily, R. K., and Daily, L.: The modern technique in the treatment of amblyopia. Am. J. Ophth., **49**:136, 1960.
4. Urist, M. J.: Eccentric fixation in amblyopia ex anopsia. AMA Arch. Ophth., **54**:345, 1955.
5. Guibor, G.: Eccentric fixation. Am. J. Ophth., **27**:989, 1944.
6. Folk, E.: Personal communication.
7. Chavasse, F. B.: Worth's Squint. Philadelphia, Blakiston, 1939, p. 535.
8. Harms, H.: Arch. f. Ophth., **138**:149, 1944.

LIMBOSCLERAL TREPHINATION*

H. Saul Sugar, M.D.
Detroit, Michigan

Dissatisfaction with the relative frequency of late infection following corneoscleral trephination and the consequent search for a safer yet effective method have led to an operative procedure which is simpler, certainly as effective, and probably safer than the classical procedure of Robert Henry Elliot. In a sense it is a return to the original so-called scleral trephining. Experience with 20 such operations with a follow-up of two to 12 months is believed to warrant this report.†

In the classical Elliot operation, the conjunctival flap dissection is continued into the cornea for about a mm. The two-mm. trephination is then made so it is half in clear cornea and half in limbus. The flap on its corneal half is thus a thin layer in which no Tenon's capsule is present. Very frequently the resulting filtering bleb becomes extremely thin, particularly at the corneolimbal junction. This is true even when the classical corneal splitting is carried out as directed by Elliot, namely, splitting the cornea so that the corneal flap includes not only the epithelium and Bowman's membrane but also some of the superficial corneal lamellae.

The presence of a thin covering on the anterior portion of the trephine bleb is believed to be responsible for the relatively high incidence of late infection after trephination as compared to its low incidence after iridencleisis operations in which the only differences appear to be the presence of Tenon's capsule under the conjunctiva throughout its extent and the more posterior location of the incision in the latter procedure. As a matter of fact, an abrupt ledge often appears at the anterior edge of the trephine bleb while the iridencleisis bleb is usually smoother. The obvious question arising from the difference in the blebs following the two types of operations is: Do we need to go beyond the corneolimbal margin in doing trephining? Elliot laid stress on the importance of the trephination being made well forward so that the removed button would include a complete disc of Descemet's membrane and not encroach on the trabecular area. I believe that this admonition by Elliot was baseless as far as involvement of the trabeculae is concerned but it has influenced ophthalmologists for over 50 years.

A few years ago Dr. Lorenz Zimmerman of the Armed Forces Institute of Pathology requested that trephine buttons be sent to him for use in studies of the trabeculae. I was surprised to learn that practically none of the buttons showed trabeculae or even Schwalbe's line. I realized that they were too far forward for this.‡

Later, in studying sections of Eye-Bank eyes as part of a study of the white limbus girdle of Vogt, I found that the limbus, especially in the upper portion of the eye, varies considerably in width so that the sclerolimbal junction may be one to three mm. or more behind the corneolimbal border. Likewise, we know from gonioscopy that the position of the angle recess varies considerably, depending on the axial length of the eye particularly.

It occurred to me that one might be able to do the trephining operation without corneal splitting wherever the limbus was wide enough. I reasoned that in dealing with simple glaucoma where no peripheral an-

* From the Sinai Hospital of Detroit and Wayne State University College of Medicine. Presented in part and demonstrated at the Eye Surgery Refresher Course, University of Toronto, April 5, 1960.

† At the time of proof-reading, these cases had been followed eight to 18 months.

‡ Continued studies of trephination buttons even after using the technique described herein indicated that trabecular tissue is only occasionally found in the buttons, possibly because the trabecular area is torn free of the button and is possibly removed separately in some cases.

terior synechias are present, transillumination of the upper angle from below should show where a two mm. trephine would avoid the ciliary body. At first the trephining site was located just behind the corneolimbal junction, at the widest portion of the limbus above, either central or to either side of center. Subsequent trial resulted in placing the anterior edge of the trephine about one-third to one-half mm. behind the corneolimbal junction to avoid cutting the Tenon's tissue insertion. In every instance the anterior chamber was entered without exception.

We have known the approximate distance between the corneolimbal junction and the chamber angle for many years. Rochon-Duvigneaud[1] found the interval between the edge of the transparent cornea and the chamber angle to be 2.75 mm. above, 2.0 mm. below and 1.25 mm. on the side in the horizontal axis. Barraquer[2] found the permissible trephine space to be 2.0 mm. Ducamp[3] found the interval to be 2.25 mm. between the corneolimbal junction anteriorly and the insertion of the ciliary body posteriorly. He found that the orifice produced by a 2.0-mm. trephine was slightly smaller than the trephine employed. Yet he agreed with Elliot that inclusion of the cornea in the trephined area was necessary. Lagrange[4] gave the following figures for the distance between the iris root and the corneolimbal junction: 1.75 mm. above, 1.45 mm. below and 1.0 mm. at the sides.

In preparing this paper, I found that Sobhy Bey,[5] in 1921, made some observations which were similar to mine. He objected to corneal splitting in order to avoid the thin covering of the trephine hole produced thereby. He stated:

> After examining the sections of a good number of globes that were trephined according to the technic given by Elliot, I have found that the trephine hole is unnecessarily far away from the angle of the anterior chamber and this at once has drawn my attention to the scleral overlapping which might deceive the operator. I thought in these cases the splitting or the cutting of the cornea during the operation unnecessary and the hole could have been in the right place without it. On the other hand I met with cases in whom the scleral overlapping is broad enough to allow the insertion of a medium-sized trephine 1.5 mm without corneal dissection. I was always tempted to stop the corneal dissection in my technic for Elliot's trephining and owing to the lack of experiments and not forgetting the objections Fergus's trephining had, I dared not stop it and feared touching the ciliary body by being so peripheral.

Sobhy Bey concluded from experiments on two globes before enucleation that no corneal splitting is necessary if a 1.5-mm. trephine is used and if the scleral overlap is 1.75 to 2.0 mm.; if only 1.0 mm. overlap is present, he deemed corneal splitting necessary.

A brief review of the history of trephination for glaucoma will serve to give proper background for the operation to be described. The first operations were scleral trephinings. Argyll Robertson,[6] in 1876, described the use of a one-twelfth inch trephine in four cases to allow vitreous to escape through an incision in the pars plana. Blanco,[7] in 1903, and Frohlich,[8] in 1904, made 4.5 mm. and 5.0 mm. diameter sclerectomies, respectively, under conjunctival flaps. These operations soon lost any adherents.

The first trephining involving the anterior chamber was that of Fergus who, in spite of Elliot's claims, deserves credit for the introduction of the trephining operation. In January, 1909, Fergus[9] introduced his operation in which, after preparing a large conjunctival flap, a three mm. Bowman's trephine was used to make a sclerectomy beginning as close to the cornea as possible. In Fergus' words, "the operation does not involve the ciliary body at all but lays it bare." After doing a simple trephining in three cases he subsequently added the introduction of the point of a fine iris repositor into the anterior chamber through the scleral opening. Fergus considered his operation as a modification of the Lagrange sclerectomy, as indeed it was.

Elliot and Treacher Collins[10] described the modified Fergus operation as a combination of trephining and cyclodialysis. In fact, Elliot emphasized the cyclodialysis part of the operation in such a way as to indicate that

his own claim to priority in introducing the trephining operation was thus made more valid. Although Fergus agreed with Treacher Collins' description of a portion of Fergus' operation as cyclodialysis, the descriptions of Fergus himself indicate a different concept of cyclodialysis than that which is held today. As a matter of fact, I personally doubt whether a true separation of the ciliary body resulted. At any rate, Fergus, in spite of Elliot's claims to the contrary, deserves priority for trephining into the anterior chamber, although both men deserve to be honored as pioneers in this operation.

Elliot[11] introduced his trephining operation in August, 1909, and described its use in 50 cases. A large triangular flap based at the limbus was prepared (fig. 1-A) and a two-mm. trephine was placed as close to the limbus as possible after baring the scleral tissue. An iridectomy was made in about one fifth of the cases.

In subsequent operations Elliot[10] greatly modified his operation into the corneoscleral trephining as we know it today. Instead of using a triangular flap with the incision beginning and ending at the limbus, he changed the flap to a large one with the incision running concentric with the limbus in its central area and located eight mm. from the cornea (fig. 1-B). The flap was continued into the cornea by splitting the latter with the points of closed scissors or a splitter starting just behind the line of reflection of the flap. The cornea was split for a distance of one mm. The trephining was made just above the distal end of the flap. An iridectomy was usually made and the flap then replaced and sutured.

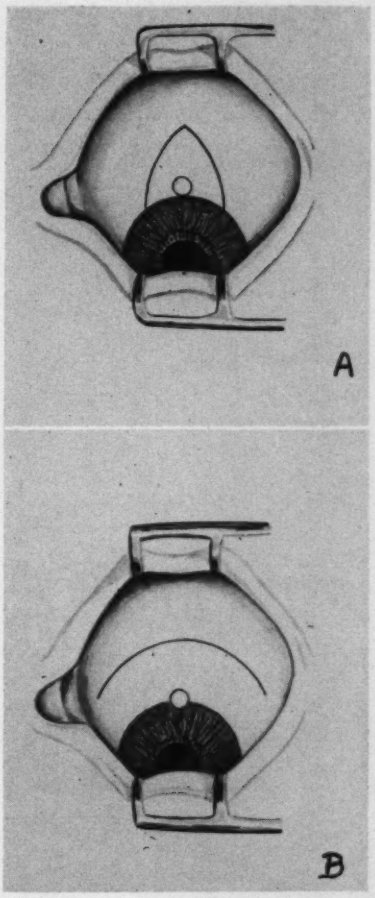


Fig. 1 (Sugar). (A) Trephining operation originally used by Elliot. (B) Trephining operation as modified by Elliot to include corneal splitting.

Limboscleral trephination

The operation which I term limboscleral trephination or limbosclerectomy is essentially a modification of the earliest Fergus and Elliot operations (fig. 2). It may be considered under the headings of anesthesia, flap, trephining, iridectomy and conjunctival wound suture.

Anesthesia

Local anesthesia with cocaine drops is followed by the injection of a small quantity of Xylocaine (one percent) at the external canthus and under the superior rectus muscle, ballooning out the upper conjunctiva. A retrobulbar injection of the same drug is usually used.

The flap

The flap should be large to avoid a scar which would limit the filtration of fluid to

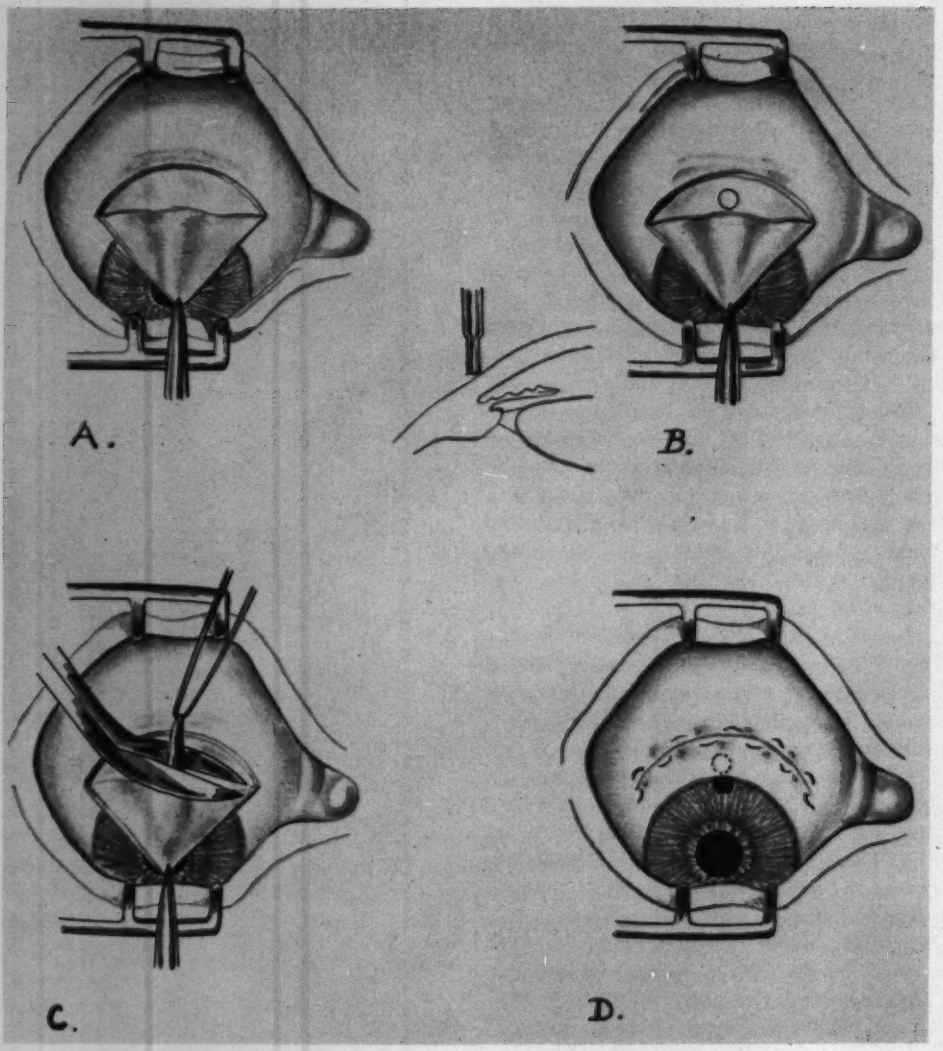


Fig. 2 (Sugar). Limboscleral trephining operation. (A) Conjunctival flap drawn down from above after infiltration with local anesthetic. (B) Trephining just above the corneolimbal margin. Inset diagram shows forward tilt of trephine blade to insure posterior hinge. (C) Peripheral iridectomy after removal of limboscleral button. (D) Appearance after suturing flap in two layers.

too small an area. The incision should be about 16-mm. long and be concentric with the limbus beginning just in front of the superior rectus insertion and enlarging it to each side. The conjunctiva and subconjunctival tissue are grasped just in front of the insertion of the superior rectus muscle. The conjunctival incision should be made first, then Tenon's capsule is cut separately. The flap is turned back over the cornea and the sclera is bared to the limbus, using the tips of closed scissors with slightly blunted points

to scrape the sclera to both sides, beginning at the central area. The bare area of limbus usually is seven or eight mm. in length. The insertion of Tenon's capsule is separated from the sclera only up to about one-third mm. from the corneolimbal junction. A cotton-tipped applicator is used to hold the flap over the cornea to lay bare the limbus.

The trephining

The anterior edge of a 1.5 or 2.0-mm. trephine blade is applied just above the insertion of Tenon's capsule, usually about one-third mm. from the corneolimbal junction. The trephine is then tilted forward slightly so that the disc of limboscleral tissue will be hinged on its scleral side. The moment the trephine cuts through into the anterior chamber there is a sudden upward jerk of the upper pupil border, producing a pear-shaped pupil. The trephine is removed. The button of sclera is usually pushed upward in its unhinged portion by the prolapsing iris. The button is removed by cutting across its hinge. If the hinged portion is located over the anterior portion of the ciliary body or if peripheral anterior synechias involve the functional posterior two thirds of the trabecular area, the button may be cut across so as to avoid disturbing the posterior area involved with the synechias or the ciliary body.

In a similar manner one may limit the size of the opening by cutting across the button at any desired level, leaving the hinged fraction in place. This might be desirable where a trephining operation is to be performed in a case of subacute angle-closure glaucoma where too large an opening might lead to delay in formation of the anterior chamber. Trephining is not advisable in acute angle-closure glaucoma with high tension at the time of operation since the rapid evacuation of aqueous might further displace the lens forward and might lead to malignant glaucoma.

It should be pointed out that a punch forceps inserted through an incision placed where the anterior trephine edge is placed in the operation described here produces a posterior lip sclerectomy which differs in no way in its effect. The blade of the punch forceps is inserted only as far as the angle recess. Like the trephine, it may cut off the insertion of the ciliary muscle if it reaches the angle recess.

The iridectomy

If the operation has gone well a fairly large iris bulge is present. Its dome may be excised with scissors blades held horizontally after grasping the iris with forceps. However, if the trephine has been tilted backward slightly, the blade may cut through the iris and no prolapse will occur. An attempt should be made to grasp it with forceps but if this cannot be easily done, no further attempts should be made. Elliot made an iridectomy in only 21 percent of his first 50 cases and then only to prevent iris incarceration in the wound. It should be pointed out here that since the trephining is made farther back on the globe than with Elliot's operation, there is less danger of injury to the crystalline lens. This peripheral location might also be important in preventing the pupil block which may result in malignant glaucoma.

If the iris is cut while removing the trephine button, it may fall back and be difficult to remove. Here again, if not easily grasped it is better to cease trying. If the pupil is bound down by posterior synechias and the iris does not prolapse, it is not necessary to have an iridectomy.

It is important, after iridectomy, to be sure the pupil is returned to its round shape and to make certain that no iris incarceration is present in the trephination: This is done by gently lifting the anterior lip to release the iris and then massaging the cornea with a cyclodialysis spatula. Usually when the iris is released the pupil promptly assumes a round position and, since the trephination is made more peripherally, the iridectomy is easily seen.

TABLE 1

MEASUREMENTS OF DISTANCE FROM CORNEOLIMBAL JUNCTION TO THE INSERTION OF CILIARY MUSCLE, THE IRIS RECESS AND THE END OF DESCEMET'S MEMBRANE IN EYE-BANK EYES

Eye Number		1	2	3	4
		mm.	mm.	mm.	mm.
Corneolimbal junction to insertion of ciliary body in scleral spur	Above	2.5	1.7	1.7	1.6
	Below	1.4	1.5	1.1	1.5
	Side	1.2	0.75	0.9	0.5
Corneolimbal junction to depth of iris recess	Above	2.6	1.8	1.8	1.7
	Below	1.6	1.6	1.4	1.5
	Side	1.2	1.0	1.0	0.5
Corneolimbal junction to end of Descemet's membrane = "overhang" of limbus	Above	1.0	1.1	1.2	0.9
	Below	0.9	0.4	0.6	1.0
	Side	0.8	0.5	0.3	0.16

Each measurement is an average of three or four sections.

SUTURING OF THE CONJUNCTIVAL FLAP

After the conjunctival flap is replaced, a 6-0 catgut suture is used to close the Tenon's capsule layer from one side to the other, then return in the conjunctival layer, finally tying the two ends of the suture together. Although it is a continuous suture it is locked at regular intervals. Atropine is instilled after the suturing is completed.

STUDIES OF THE LIMBAL OVERLAP

Experimental trephinations were made on four Eye-Bank eyes of average axial size to show the location of a two-mm. trephining in relation to the trabeculae, ciliary body, scleral spur and angle recess as well as to the corneolimbal junction. A superficial cut was made at the corneolimbal junction. A trephine hole was then made in the limbus of each eye in the 12-o'clock, 6-o'clock and in the temporal horizontal positions. Sections of these globes containing the trephined areas were then made and studied.

Microscopic measurements with a graticule were made of the distances between the projection of the corneolimbal junction and the insertion of the ciliary body, the depth of the iris recess and the end of Descemet's membrane. It was found that the cut made at the corneolimbal junction corresponded within 0.2 mm. to the end of Bowman's membrane.

As shown in Table 1, there is considerable variation in measurements in the small number of eyes. The distances were practically all greater above, less below and least at the sides. The most important values are the extent of limbal "overhang" which amounts to about 1.0 mm. above, and the distance between the corneolimbal junction and the scleral spur which varied between 1.6 and 2.5 mm. in these four eyes.

The distance from the corneolimbal junction and the iris recess is slightly greater. These figures indicate that a 1.5-mm. trephine placed a short distance behind the corneolimbal junction will generally avoid the insertion of the ciliary body at the scleral spur. A 2.0-mm. trephine so placed often uncaps the anterior portion of the ciliary muscle. If the trephine button is hinged and is cut across, as already described, there is no danger of injury to the ciliary body. The limited distance below and especially at the sides of the cornea indicate the danger of

using the above technique at these sites in most eyes.

In the series of clinical cases not a single instance of visible injury to the ciliary body occurred. Gonioscopy in each case showed an open trephine hole and a free iris opening, with the exception of one in which there was an adhesion of a thin ciliary process to one wall of the trephine hole. The bleb was normal in this instance. Ciliary processes were visible through the iris opening in each case. It must be emphasized that the button was cut off across the hinge in each instance so that the trephine hole thus made with a two-mm. trephine measures less than two-mm. in its vertical meridian. As a matter of fact, complete trephine holes made in the sclera experimentally in enucleated eyes and using a two-mm. trephine, measure less than that after removing the button if the trephine blade is dull but not if the blade is sharp.

Clinical results

Twenty limboscleral trephinations have been used as the basis of this paper. The first was done 12 months ago, the last two months ago.* Of the 20, 18 were in eyes with simple glaucoma in which medical treatment with miotics, carbonic anhydrase inhibitors and epinephrine bitartrate was ineffective. All of these had excellent results, the tension being lowered to 18 mm. Hg or below (1955, Schiøtz) in each case. The blebs were smoother, with the characteristics of good iridencleisis blebs as far as their noncystic nature was concerned.

One trephination was done on an eye with chronic angle-closure glaucoma in which a previously done peripheral iridectomy was ineffective. Synechias covered the posterior two thirds of the trabecular wall. The trephination was done in the upper nasal quadrant, with the trephine cut carefully observed until the anterior half was open and the iris prolapsed. The button was then transected, leaving the posterior half intact. In this way the synechias were left undisturbed. The tension was reduced to 17 mm. Hg.

The remaining case was performed on a patient with unilateral glaucoma which followed repeated episodes of acute iritis associated with hyphema. These episodes occurred six times over a period of 12 years, the last episode in 1958. The angle was open. The coefficient of outflow was 0.05. The blindspot was markedly enlarged. The operation was uneventful but the conjunctiva appeared to scar down and the tension became elevated to 24 mm. Hg (1955 Schiøtz). Miotics were then used. Gonioscopy showed an open trephination and angle.

Complications

Delayed reformation of the anterior chamber occurred in two cases, one for four days, the other for 10 days. The results were unaffected. Hypotony did not appear in any case after the healing period of about two weeks. This incidence of delayed reformation is approximately the same as in the trephination done by the corneal-splitting technique. Elliot, in his early 50 cases, found delayed reformation for four to 12 days in eight cases.

Summary

A new or rather a return to an old technique of limboscleral trephining is described. Its efficacy, ease of performance and promise of increased safety are points in its favor. In 20 cases, it was completely effective in 19 and failed in one unilateral secondary glaucoma which had followed repeated episodes of hemorrhagic iritis. Because of the possibility of controlling the size of the trephine opening by transecting the hinged button, the operation may be used in nearly all instances where external filtration is desired except in acute, unrelieved angle-closure glaucoma.

18140 San Juan (21).

* At the time of proof-reading, the follow-up is eight to 18 months. The results remain the same. Twelve more cases have been done, all successful without miotics.

References

1. Rochon-Duvigneaud: Recherches sur l'angle de la chambre anterieure et le canal de Schlemm. Paris, G. Steinheil, 1892.
2. Barraquer, J.-A.: Sur l'operation d'Elliot. Clin. Ophtal., **19**:129, 1913.
3. Ducamp, A.: La trepanation corneo-sclerale d'Elliot, Paris, 1913.
4. Lagrange, F.: Du glaucome et de l'hypotonie. Paris, 1922.
5. Bey, S.: The sclero-corneal junction, Bull. Ophth. Soc. Egypt, **1**:40, 1921.
6. Argyll-Robertson, D.: Trephining the sclerotic: A new operation for glaucoma. Royal London Ophth. Hosp. Rep., **8**:404, 1876.
7. Blanco: Sitzungsberichte Int. Med. Kongress, Madrid. Klin. Monatsbl f. Augenh., **41**:150 (Pt. 2) 1903.
8. Frohlich, K.: Ueber die Trepanation der Sklera bei schmerzhaften Glaukomblindheit. Klin. Monatsbl. f. Augenh., **42**:411, 1904.
9. Fergus, F.: Treatment of glaucoma by trephining. Brit. M. J., **2**:983, 1909.
———: Trephining for glaucoma. Ophthalmoscope, **8**:74, 1910.
———: Glaucoma and trephining. Ophth. Rev., **34**:129, 202, 1915.
10. Elliot, R. H.: A treatise on Glaucoma. London, Henry Frowde & Hodder & Stoughton, 1922, ed. 2.
11. ———: A preliminary note on a new operative procedure for the establishment of a filtering cicatrix in the treatment of glaucoma. Ophthalmoscope, **7**:804, 1909.

STREPTOTHRIX CANALICULITIS*

PHILIP P. ELLIS, M.D.
Denver, Colorado
AND
SYDNEY C. BAUSOR, PH.D., AND JOHN M. FULMER, M.D.
Little Rock, Arkansas

Introduction

Streptothrix canaliculitis, the popular name given an infection of the canaliculi with actinomycetes, is a well-known disease that was first described by von Graefe a little over 100 years ago.[22] Though this infection is fully recognized, it is quite uncommon and often undiagnosed.

The etiology of streptothrix canaliculitis is mostly presumptive. It is based on the association of conglomerations of an actinomycete in the enlarged canaliculi and diverticula therefrom, with clinical symptoms of tearing, persistent inflammation of the punctum and medial conjunctiva and a mucoid or mucopurulent discharge.

The conglomerations have been termed "concretions" but have been shown, when investigated,[17, 11] as in our studies, to be a mass of branched mycelia of an actinomycete. Concretions may also be found in the lacrimal sac and nasal lacrimal duct.[9] The concretions are soft and readily crushed under a coverslip. When cultured, the organism composing the concretions is characterized by a wide range of pleomorphism in which a branched mycelium without demonstrable cross walls, fragments into bacilli or filaments. In addition, small cocci form in a string resembling a miniature Streptococcus, about the same diameter as the hyphae or the separated bacilli, that is, about 1.0 μ. These three conditions may be found concurrently or one or the other may prevail.[18, 20] Structures described as "symplasia" have also been reported[23] which are large masses, plasmodial-like in appearance, containing numerous stainable regions.

The name, Streptothrix, has become widely accepted in clinical medicine through long usage to designate the microorganism associated with actinomycosis in man and the bovine. Its historical background lends precedence to its usage. The concretions found in

* From the Division of Ophthalmology, Department of Surgery, University of Arkansas Medical Center, Little Rock, Arkansas.

the lacrimal canaliculi were first described as Streptothrix foersteri by Cohn in 1875.[6] The organism was described and named from direct observation as it appeared in the morbid process. It was an unfortunate choice which led to later confusion since the name Streptothrix was previously applied to a genus of true fungi. This made the name invalid according to rules of nomenclature. Nonetheless it came into accepted usage and has remained so to the present day. Concretions were observed by Cesoni in 1670,[5] 205 years before Cohn described their nature, and they were again observed in 1854 by von Graefe. It should be mentioned that these concretions are comparable in nature to the sulfur granules found in lumpy jaw (actinomycosis) in cattle, caused by the same or very closely related organism, which was described by Harz in 1877 as a branched mycelium to which he applied the name Actinomyces bovis.[12] He recognized its similarity to Cohn's Streptothrix.

The organism found in lacrimal canaliculitis in man is now also relegated to the genus Actinomyces and usually designated as a strain of A. israelii, although the difference between Actinomyces bovis and Actinomyces israelii is not sharp and definitive. They are antigenically different, but otherwise quite similar which probably justifies the clinical use of Streptothrix, for the name originally described the microorganism as a morphologic entity in the special ecologic environment of man as the host.

Clinical features

The clinical features of Streptothrix canaliculitis are: (1) persistent tearing, (2) chronic inflammation of the medial conjunctiva, (3) prominence and redness of the punctum, (4) mucoid or mucopurulent discharge, and (5) swelling and tenderness of the canaliculi.[1,3,7,8,13] These symptoms may develop over a period of years and may or may not be associated with one another at all times. However the more apparent conjunctivitis may obscure the presence of a canaliculitis, and treatment is often directed only toward the conjunctivitis.[10,18]

Nearly all cases occur in women. Usually only one canaliculus is involved but in about 30 percent both canaliculi are infected. Despite the fact that there is tearing, one can usually irrigate the lacrimal passages without a great deal of difficulty. On attempted probing of the passages one may encounter mild obstruction although this has not been a characteristic finding in our experience. Milking of the involved canaliculus toward the punctum causes the expression of a creamy exudate.

These characteristics are sufficient for a well-founded diagnosis of Streptothrix canaliculitis. Cursory bacteriologic examination may be misleading because of the pleomorphism of the organism.

Bacteriologic analysis

If a bacteriologic analysis is limited to the study only of stained smears of exudate from the punctum, the data secured may be misleading and result in more confusion than aid. The pleomorphism of Actinomycetes israelli attributes in no small way to this. Pus usually occurs in abundance, and either within the pus cells or outside may be found only a few microorganisms. These may appear to be streptococci and so diagnosed. On the other hand, few or abundant diphtheroids may be found which on direct examination alone cannot be directly related to the actinomycete. They may be species of the Corynebacteriaceae or members of the Lactobacillaceae.[2] It is only when branched filaments are also found that a positive correlation is possible between clinical symptoms of streptothrix canaliculitis, upon which a diagnosis can be hazarded, and its confirmation based upon known etiology. Typical threads of diphtheroids may or may not appear.[15,16] The difficulties in laboratory diagnosis are well borne out in the detailed bacteriologic analysis performed in our latest case. This particular case lent itself to detailed bacteriologic studies because even though a correct diagnosis was

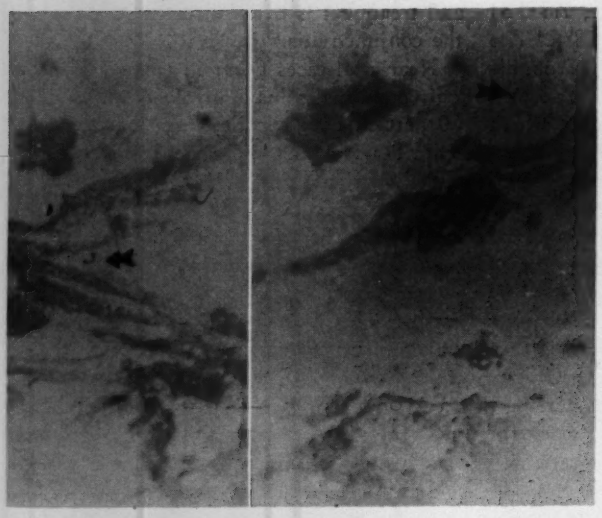


Fig. 1 (Ellis, Bausor and Fulmer) Smear showing pus cells, mucin threads and rare occurrence of bacilli and short chain (×1,125).

made early, a cure was not obtained until repeated surgical procedures were performed.

In the case of the patient studied in detail, smears, taken prior to the first surgical treatment, showed among the pus cells a number of diphtheroids. The latter are bacilli which remain attached to one another in twos, threes or more, but usually at only one point. This allows the attachment to function as a hinge and the rods assume angles to one another. No filaments were observed. Prior to reoperation, four months later, direct smears showed an entirely different picture with many pus cells but few bacteria. The bacteria discovered appeared like small streptococci and might casually have been diagnosed as a streptococcal infection. There were also a few scattered gram-negative rods (fig. 1).

However, cultures of the exudate, expressed from the punctum, revealed the true nature of the microorganism associated with the inflammation. Fluid thioglycollate was the preferred medium for initial isolation. In 48 hours at 37°C. minute colonies appeared in the anaerobic zone of the tube. They increased in size and in about nine days resembled the concretions later found in abundance within the canaliculi, grossly and microscopically.

Colonies were picked and subcultured on both fluid thioglycollate and the thioglycollate medium solidified with 1.5 percent agar-agar. On solid medium the colonies were of the rough type. Microscopically they were composed of a typical actinomycete mycelium, sparsely branched with numerous inter-

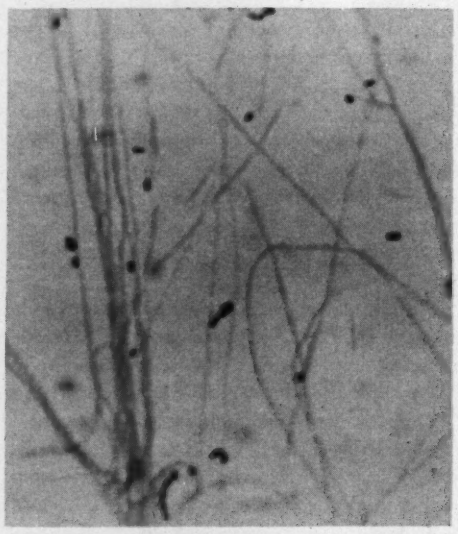


Fig. 2 (Ellis, Bausor and Fulmer). Twenty-four-hour culture, exhibiting long unbranched filaments and formation of "streptococci" (×1,125).

spersed "streptococci" (fig. 2). The "streptococci" were of the same diameter as the mycelium, and represented short branches of the latter which became organized into spherical segments and subsequently detached themselves from the hyphae bearing them (fig. 3). The "streptococci" are thus actually arthrospores or oidiospores, and account for the simulated aspect of streptococcal infection found on the initial smear. Also, bacilli and short unbranched filaments were present that resulted from fragmentation of the mycelium (fig. 4).

Upon surgical exposure of the canaliculi and lacrimal sac concretions were secured for study. The concretions were irregular in general form, creamy white in color. Their surface was warty, that is, composed of microscopic mounds with rounded ridges. When crushed, the mass of interwoven mycelium became apparent, but swellings of terminal filaments were not noted (figs. 5 and 6).

The filaments stained gram negatively and associated with them were chains of cocci of approximately the same diameter as that of the hypha. The cocci stained gram positively. The concretions are actually a colonial mass of interwoven hyphae.

Slide cultures of the concretions in thioglycollate or in indole nitrite broth, incubated anaerobically at 37°C., showed the typical outgrowth of mycelium with detached "streptococcal" branches. Also surrounding the concretions small colonies of cocci de-

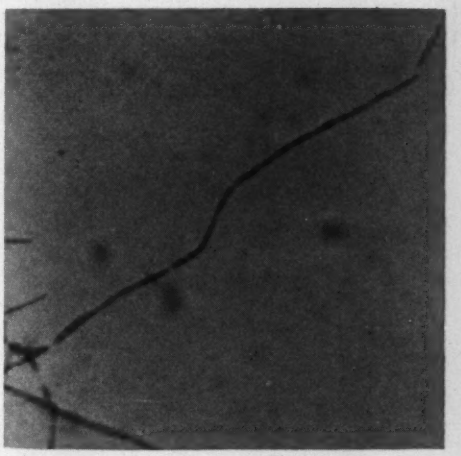


Fig. 4 (Ellis, Bausor and Fulmer). Four-hour culture, showing fragmentation of mycelia into bacilli and diphtheroids (×1,125).

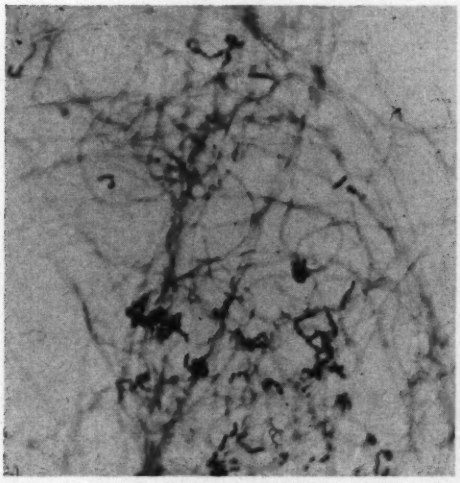


Fig. 3 (Ellis, Bausor and Fulmer). Four-hour culture of Actinomyces israelii, demonstrating development of "streptococci"-like oidia and gram-variable mycelia (×1,125).

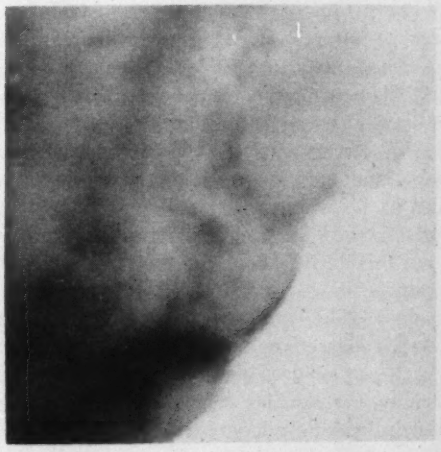


Fig. 5 (Ellis, Bausor and Fulmer). Enlargement of limb of concretion, showing rounded ridged surface (×300).

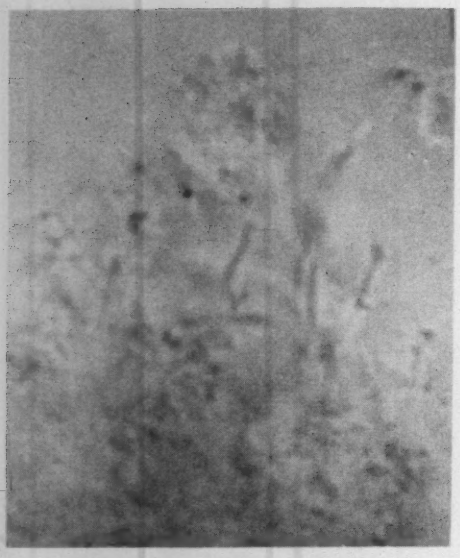


Fig. 6 (Ellis, Bausor and Fulmer). Enlargement of edge of concretion, revealing a mycelial mat (×1,125).

veloped by budding of the "streptococci," especially in indole nitrite. Tube cultures were apparently identical with the organism isolated from the exudate. In no case were swollen hyphal tips observed, either in concretion or in culture.

The strain of actinomycete isolated here was of interest in its gram reaction. The branched mycelium and fragmented bacilli and filaments were gram negative when examined after 24 or 48 hours. The "streptococci" were gram positive. When subcultures were examined in four hours both mycelium and bacilli were gram positive and frequent cells showed the transition to gram negative even this early. These had granular areas of gram positiveness on a gram-negative background. The gram-negative bacilli which often appeared in pairs, and in this strain had more or less pointed ends, showed a striking resemblance to fusiform bacilli with which they might have been readily confused were one not aware of their origin (fig. 7). However, this strain did not grow on crystal violet medium. Distinction between the fusiform bacillus and the Actinomyces may be made by growth on crystal violet media.[4] The fusiforms grow as purple convex colonies, whereas the actinomycete is inhibited.

Serial dilutions of dihydrocortisone acetate, from 22V/ml. to 1.25V/ml., added to thioglycollate cultures showed no appreciable effect on the growth rate of this strain. The details of this study and of the effects of antibiotics will appear in a subsequent communication.

The organism was nonacid fast, catalase negative, anaerobic with slight growth under nitrogen, carbon dioxide being necessary in the gaseous environment, optimum temperature at 37°C. nonhemolytic. It did not grow on nutrient gelatin. Acid without gas developed from dextrose fermentation. Morphologic, cultural and pathologic characteristics all point to this organism as being Actinomyces israelii.

Treatment

The treatment of streptothrix canaliculitis may be mechanical, medical or surgical or a

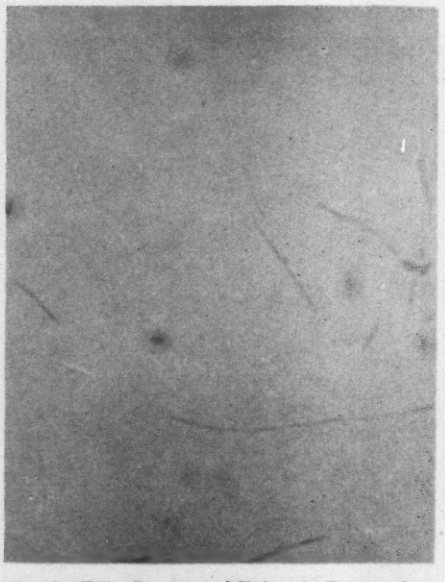


Fig. 7 (Ellis, Bausor and Fulmer). Twenty-four-hour culture, demonstrating gram-negative fusiform-like bacilli and filaments (×1,125).

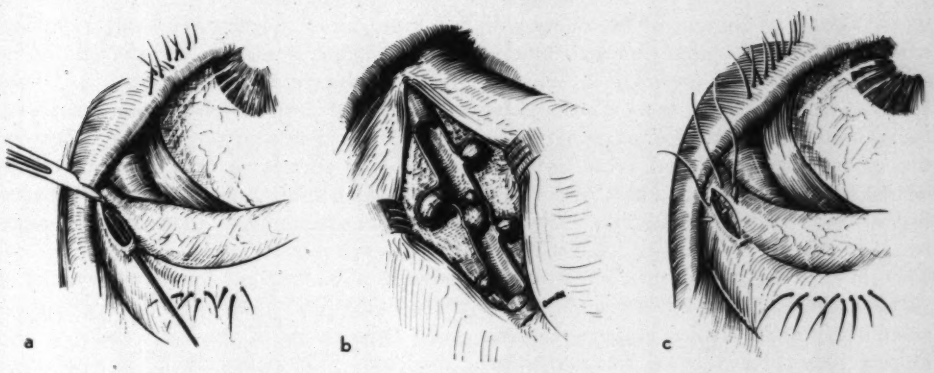


Fig. 8 (Ellis, Bausor and Fulmer). (a) Canaliculus opened by cutting down on a lacrimal probe. Punctum is preserved. (b) Multiple concretions in enlarged canaliculus and its diverticula. Concretions removed under direct vision. (c) Incision closed with interrupted chromic sutures.

combination of these three methods. The simplest form of treatment consists of dilating the punctum and expressing the concretion with pressure along the inside of the lid. A more effective way of removing the concretions is to use a small curette inserted into the canaliculus as an aid to the mechanical removal.[21] After the removal of the concretion either by stripping or by curettage, a one-percent solution of tincture of iodine or a solution of aqueous penicillin may be instilled into the canaliculus with a lacrimal syringe. Of the six cases seen by us the past few years, four cases were successfully treated by these means. One of these cases however, had a recurrence of the infection two years later.

The surgical management of these cases consists of slitting the canaliculus through the punctum and then mechanically removing the concretions under direct vision.[7] Though this is effective, it is not desirable to treat the lower canaliculus in this fashion. Cutting the punctum destroys the negative pressure and capillary traction of the drainage channel. We have recently attempted to overcome this objection by modifying the technique of slitting the canaliculus. Instead of cutting through the punctum, an incision is made into the canaliculus by cutting down on a probe inserted into the canal. The incision is made on the conjunctival side of the lid approximately two mm. behind the margin. The punctum is preserved. After the concretions are removed the incision is closed with interrupted 6-0 chromic sutures (fig. 8). We have employed this procedure on two occasions and found that the drainage system of the lower punctum and canaliculus functioned well after healing took place.

On one occasion we had recurrence of the actinomycotic infection in a canaliculus approximately four months after complete surgical removal of the concretions followed by the application of mild iodine solution. At the time the canaliculus was re-explored it was found that the concretions had returned and went down into the common canaliculus. At the same time an exploration of the lacrimal sac was performed through a skin incision and it was found that the concretions lined the wall of the lacrimal sac. Evidently this was the source of the reinfection of the canaliculus.

Discussion and Comments

For the practicing ophthalmologist sufficient reliance may be placed on the clinical features of the disease so that resort to bacteriologic analysis is not necessary in making a diagnosis. If a simple and quick bacteriologic analysis were available for confirmatory purposes, it would be advisable, as in the case of other infectious diseases. Incomplete bacteriologic study may mislead the physician and throw doubts on his correct clinical diag-

nosis. This is so because of the rarity with which the typical gram-positive actinomycete mycelium shows up in smears of the exudate. In only two of our six cases was the mycelium found on direct microscopic examination. In the other cases, rods and cocci were the laboratory reports, from which data it was impossible to come to a ready conclusion that we were dealing with an actinomycosis. Therefore, on the basis of the clinical diagnosis we would suggest that treatment be undertaken, either by mechanical or surgical means. During these procedures if concretions are observed, it is a certain confirmation of an actinomycotic infection since these concretions are colonies of the actinomycete.

Though this is a localized infection, topical use of antibiotic drops is not usually effective in an advanced case of streptothrix canaliculitis. Direct contact is not made with all of the organisms because of the insufficiency of penetration of the drug into the occluded canaliculus and because of the massiveness of the mycelia. However, the syringing of the canaliculus with antibiotics after the concretions have been removed, has an inhibiting effect upon the possible remaining organisms. One can speculate that with widespread use of antibiotic eyedrops, the incidence of streptothrix canaliculitis may fall. This seems highly probable since the disease is of a chronic nature and requires considerable time for the organisms to reach a state where they produce clinical symptoms. Before reaching this state the organisms might be killed off by antibiotic therapy. Others have expressed the opinion that the opposite might be true.[14, 15]

Preliminary results showed that dihydrocortisone acetate in vitro had no appreciable effect upon the growth rate of the actinomycete. Any modification of pathogenesis by cortisone must be indirect and reside in its action upon the host.

From our experience, a cure may frequently be obtained by mechanical removal of concretions plus instillation of antibiotics or mild solutions of iodine. It may be necessary to repeat this treatment several times in order to effect a permanent cure since all concretions may not be reached by the initial curettage. In obstinate cases or where recurrence of the infection takes place, a surgical approach offers the most certain opportunity to remove the concretions under direct visualization. The extent of the involvement is also disclosed. This is important since the concretions may extend down into the common canaliculus and even the lacrimal sac and serve as the nidus for reinfection. The objection to the surgical treatment may be largely removed by the technique described herein, since in this procedure, the integrity of the punctum and canaliculus is preserved and the function of lacrimal drainage is not impaired.

Summary

Actinomycosis of the lacrimal canaliculi, commonly known as streptothrix canaliculitis, can be usually diagnosed by clinical features. Superficial bacteriologic determinations may be misleading because of the pleomorphism of the organism and the infrequent appearance of the mycelial development in the smears. Since the organism is an anaerobe and slow growing, cultural studies are not always practical or available. Treatment is indicated on basis of clinical findings alone. Most cases may be cured by mechanical expression of the concretions and instillation of antibiotics or mild iodine solutions. Nonresponsive or recurrent cases should be treated surgically. A modified surgical treatment is suggested in which the punctum is left intact.

4200 East Ninth Avenue (20).
University of Colorado Medical Center.

References

1. Birge, H. L.: Ocular aspects of mycotic infection. AMA Arch. Ophth., **47**:335, 1952.
2. Breed, R. S., Murray, E. G. D., and Smith, N. R.: Bergey's Manual of Determinative Bacteriology. Baltimore, Williams & Wilkins Co., 1957, ed. 7.

3. Brickenhoff, A. J.: Actinomycosis of the inferior canaliculus. Am. J. Ophth., **25**:978, 1942.
4. Burns, R. P., Macnie, J. P., Pfeiffer, R. L., and Locatcher-Khorazo, D.: Unilateral conjunctivitis and canaliculitis due to fusospirochetal infection. AMA Arch. Ophth., **59**:235, 1958.
5. Cesoni: Mentioned by Smith.
6. Cohn, F.: Untersuchungen über Bacterian. Beiträge Ztschr. Biol. Pflanzen., **1**:141, 1875.
7. Duke-Elder, S.: Textbook of Ophthalmology. St. Louis, Mosby, 1952, v. 5.
8. Elliot, A. J.: Streptothricosis of the lacrimal canaliculi. Am. J. Ophth., **24**:682, 1941.
9. Fine, M., and Waring, W. S.: Mycotic obstruction of the nasolacrimal duct. Arch. Ophth., **38**:39, 1947.
10. Greeves, R. A.: Streptothrix conjunctivitis. Brit. J. Ophth., **36**:653, 1952.
11. Hagerdoorn, A.: Concretions in a lacrimal canaliculus caused by actinomyces. AMA Arch. Ophth., **80**:689, 1940.
12. Harz, C. O.: Actinomyces bovis: Ein neuer Schimmel in den Geweben des Rindes. Deutsche Ztschr. f. Tier-Med., **5**:125 (Suppl.) 1879.
13. McLanahan, A.: Fungus infection of the lacrimal canaliculi. Am. J. Ophth., **19**:418, 1936.
14. Moore, J. G.: Actinomycosis of the canaliculi, with invasion of the tissue in one case. Brit. J. Ophth., **36**:522, 1952.
15. Pine, L., and Hardin, H.: Actinomyces israelii, a cause of lacrimal canaliculitis in man. J. Bact., **78**:164, 1959.
16. Pine, L., Hardin, H., Turner, L., and Roberts, S.: Actinomycotic lacrimal canaliculitis. Am. J. Ophth., **49**:1278, 1960.
17. Riddell, W. J. B.: Streptothrix colonies in a lacrimal canaliculus: report of a case with note on diffraction spectrum examination. Glasgow M. J., **30**:452, 1949.
18. Smith, C. H.: Ocular actinomycosis. Proc. Roy Soc. Med., **46**:209, 1953.
19. Taylor, I. B.: Actinomycotic canaliculitis. Med. Proc., **2**:389, 1956.
20. Theodore, F. H.: Streptothrix as a cause of follicular conjunctivitis and other obscure conjunctivitis. Am. J. Ophth., **33**:1225, 1950.
21. Thygeson, P.: The Eye and Its Diseases. Edited by C. Berens. Philadelphia, Saunders, 1949.
22. von Graefe, A.: Koncretionen im unteren Thränenröhrchen durch Pilzbildung. Arch. f. Ophth., **1**: 284, 1854.
23. Waksman, S. A.: The Actinomycetes: Vol. I, Nature, Occurrence and Activities. Baltimore, Williams & Wilkins Co., 1959.

RESULTS OF TREATMENT OF TRAUMATIC CATARACT IN CHILDREN

ALFRED J. MCKINNA,* M.D.
Baltimore, Maryland

Children frequently suffer eye injuries which result in the development of traumatic cataracts. The management of such cases is given very little space in any of the standard textbooks and a short paragraph usually states that such a case is a highly individual problem. Reports in the literature are infrequent. This paper will deal with the excerpts in the literature and with the results of cases treated at two university centers over a 20-year period starting in 1937. Cases were taken from the records of two of the teaching hospitals of McGill University, Montreal—the Montreal General Hospital and the Montreal Children's Hospital—and from the University of California Medical Center, San Francisco.

If one surveys the ophthalmologic literature from the turn of the century, one is startled by the lack of reports on this condition as well as by their pessimism.

In 1900, Baudry wrote "Beware of traumatic cataracts; they accompany traumaticisms in all their varieties and are frequently associated with all their consequences. It is the half successes and the failures which make up the balance sheets of the operative treatment of traumatic cataract. In general, every injury to the crystalline lens should be considered as a serious menace to the existence of the eye."

In 1921,[1] Juler reporting on 20 cases of

* Former Resident Staff, Montreal General Hospital, Montreal, Canada; 1959-60 Heller Scholar in Ophthalmology, University of California Medical Center, San Francisco.

TABLE 1

ANALYSIS OF 25 CASES OF TRAUMATIC CATARACT FROM MONTREAL (1937–1958)

Age (yr.)	No. Patients	Operations		Deviations	Vision	Comment
		1	2+			
2	1		1	1	HM	
3	2		2	1	HM	
4	7	1	5	4	HM and	(1—20/30) (1—20/70—??)
6	2	1	1	1	HM	
TOTAL 2–6	12	2	9	7	HM	
7	1	1		1	4/60	(Ac. tension)
8	2	1		1	(1—HM)	(1—20/30 spontaneous)
9	2	2			HM	
10	1	1			20/70	
11	4	3	2	3	(3—HM)	(1—20/20)
12	1	1			CF 8′	
13	2	2			(1—20/20)	(1—HM)
TOTAL 7–13	13	11	2	4	20/20 to	LP only.

traumatic cataracts in children treated at the Moorfield's Hospital between 1910 and 1917 said that none of the children under six years of age had vision as good as 6/60.

In 1938,[2] Clapp of the Wilmer Institute, Baltimore, reviewed 90 cases of traumatic cataract admitted to that institution, the average age being 26 years, and reported that approximately one third retained "useful vision."

In 1943, Black[3] reporting to the Ophthalmological Society of the United Kingdom reviewed 100 cases of traumatic cataract seen at the Leeds General Infirmary during the preceding 10 years. These patients were of all ages. He found that of the first 65 cases, 43 percent of the eyes had to be removed within one year of injury. Of the last 35 cases, 19 percent were lost. He believed that the evolution of the case was largely completed within one year, often less. After this period the changes are comparable to those arising in a normal eye. He reported that a majority of the cases showed deviation, nearly always divergent, and that this persisted despite the treatment producing a clear pupillary area and good corrected vision. He concluded that more than 50 percent of the cases had vision no better than "hand movements" and that Baudry's statement concerning the "existence of the eye" was still true.

The following clinical records were then made from the hospitals already listed. The children were divided into two age groups: (I) patients aged six years and under at the time of injury; (II) those aged seven to 13 years at the time of injury.

This division was made because of the problem of amblyopia of disuse in the age group of six years and under.

I. PATIENTS AGED SIX YEARS AND UNDER AT TIME OF INJURY

(12 cases—Montreal)

CASE 1

R. W., aged four years, had a perforating injury, O.S., by a nail shot from a popgun in March, 1957. Opaque cataract developed by October, 1957, which was needled and 10 days later a linear extraction was done. Postoperatively, he was refracted and given the correcting aphakic lens and the right eye was occluded. He was unable to fix at that time but after two weeks of occlusion and with his glasses, O.S. was 20/100 (E game). Occlusion was continued one week in four, and for a longer period during the summer of 1958 when his vision was 20/40. Occlusion of the right eye was continued and he used the aphakic correction, O.S., over holiday periods since starting to school last fall. When seen in early February, 1959, his vision was 20/50 when just brought to the clinic and the aphakic correction tried. When he was occluded for a week he had little difficulty seeing 20/30+. No deviation has occurred, so far.

CASE 2

G. T. was struck in the right eye by a stone fired by a sling-shot in October, 1954, at the age of four

years. He was first seen in clinic in March, 1955, with a mature cataract, O.D., and a right esotropia. Discission was done in March, 1955, with vision of hand movements only obtained. One year later vision was not improved but his squint was corrected by a bilateral medial rectus recession in March, 1956. When last seen in November, 1957, vision was still hand movements.

CASE 3

D. W., at the age of four years suffered a perforating injury to the left eye resulting in traumatic cataract and had a discission several months later. He was not seen again until the age of 10 years when another discission was done. Postoperatively the best vision recorded was hand movements only.

CASE 4

M. R., at the age of six years had penetrating injury to the left eye with the development of cataract shortly after the injury. Discissions were done at the age of six, seven and 10 years. Now, at the age of 26 years, he has a left exotropia of 10 degrees, a clear pupillary area but the best vision obtainable is counting fingers.

CASE 5

J. S., at the age of three years, was struck in the right eye. The lens gradually became opaque and was needled at the age of six years and again at the age of 11 years. Follow-up was brief with vision recorded as hand movements only.

CASE 6

D. A., at the age of two and one-half years, was struck in the right eye by a toy, resulting in a penetrating injury to the cornea. Several months later the cataract was needled at one operation and 10 days later the anterior chamber was irrigated. A clear pupillary way was obtained but there were a few anterior synechias laterally. The best vision recorded subsequently was hand movements—poorly.

CASE 7

R. T., at the age of six years, was injured in the right eye while playing but no medical attention was sought. When first seen at the age of nine years, there were early lens changes and some vitreous strands. He returned to the clinic at the age of 12 years. At this time a mature cataract was present. A linear extraction was done with a satisfactory result only to reveal a complete retinal detachment which was described by the retinal consultant as "inoperable." Vision was light perception only.

CASE 8

M. D., in June, 1952, at the age of four years was injured when a foreign body perforated the left cornea and lens. It was removed via the posterior route at another hospital. When seen at our clinic in March, 1953, he had a mature cataract. A discission was done and at the same time some anterior synechias were freed. This did not result in a clear pupillary way, so discission was repeated in June, 1954. Postoperatively he could count fingers. When next seen in September, 1957, there were many vitreous traction bands and fundus lesions of a degenerative type, with potential retinal detachment present. The vision was now hand movements only. No deviation had occurred.

CASE 9

S. M., at the age of three years, suffered an injury of unknown type to the right eye while playing. Within one month a traumatic cataract had developed. In May, 1951, a discission was done followed in one month by a bilateral recession for esotropia. One year later the vision was recorded as 20/400. In March, 1955, he was seen with a right exotropia and right hypertropia and vision of hand movements.

CASE 10

M. D., at the age of four years, a splinter of wood perforated the left cornea and injured the lens. He was seen periodically and the eye was kept dilated for several months. He was not seen again until the age of seven years when he returned with a mature cataract. A discission was done at this time. One year later he was seen with a left exotropia of 25 degrees and vision recorded as hand movements with best correction but with multiple pinhole plus correction, 20/70? (This is as abstracted from the clinical record.)

CASE 11

E. I., in 1948, at the age of four years, was struck in the left eye by a flying paper clip. When first seen only a small vitreous hemorrhage was seen. This cleared satisfactorily and a traumatic cataract slowly developed over the next two years. At this time surgery was refused by the parents. When last seen there was a left esotropia of 35 prism diopters and vision of poor light projection. Surgery was refused because of the poor visual prognosis.

CASE 12

A. B., at the age of four years, was struck in the left eye by a stone. A discission was done three months after the injury and repeated again one year later (1936). The patient was last seen in 1958 with a left exotropia of 40 prism diopters and poor light perception. The extreme left temporal fundus showed a flat detachment with degeneration.

SUMMARY

1. Eleven of the 12 cases were reported as having vision no better than hand movements or counting fingers (one reported as 20/70 with multiple pinhole).

2. One patient had vision 20/30+. This patient had intermittent occlusion of the normal eye and aphakic correction for the operated eye immediately postoperative and intermittently for two years thereafter.

3. Six of the 12 cases developed deviation (three esotropia, three exotropia).

4. Eight cases underwent two or more operative procedures.

5. Three cases underwent three or more operative procedures.

6. Three cases subsequently developed retinal detachment. Two of these had two or more procedures; the third a single linear extraction.

7. No eyes have been lost as far as is known.

II. Patients aged six years and under at time of injury

(14 cases—University of California Medical Center)

Case 1

P. In 1929 at the age of one year, fell downstairs injuring the left eye. When first seen here in 1937 at the age of eight years there was a traumatic cataract. A linear extraction was done in May, 1937, but was followed by postoperative endophthalmitis resulting in enucleation 12 days later. Vision, nil.

Case 2

S. At the age of four years suffered a blow to the right eye which resulted in a right choroidal tear. By the age of seven years, a cataract had developed in the right eye which had become esotropic. At the age of seven years, vision was 5/200 and optic atrophy was thought to be present. No surgery was done.

Case 3

T. At the age of one and one-half years the right eye was injured in a fall. He was seen here at the age of three and one-half years with a traumatic cataract. A linear extraction was done at that time and a residual membrane was treated by discission one year later. Postoperative follow-up visits recorded vision as hand movements. No further follow-up was reported.

Case 4

B. At the age of six years was struck in the right eye by an arrow which perforated the cornea, causing an iris prolapse and rupturing the lens capsule. The lens underwent spontaneous absorption and the eye was quiet when seen in 1940. He was not seen until 1950 when he returned with glaucoma and a vision of light perception. No follow-up is reported.

Case 5

S. In 1942, at the age of five years, was struck in right eye by a stone hurled from a slingshot. One year later a discission was done with satisfactory clearing of the traumatic cataract. The best postoperative vision was hand movements.

Case 6

E. In 1944, at the age of five years suffered a perforating injury of the left cornea with rupture of the lens capsule. The anterior chamber was irrigated as an immediate procedure. The lens absorbed satisfactorily but when seen here on his last visit vision was hand movements.

Case 7

G. In 1949, at the age of three years, was struck by a stick which caused a laceration of the left cornea, resulting in small anterior synechias with a traumatic cataract. At the age of nine years, a discission was done. Postoperatively the vision was counting fingers at six feet.

Case 8

S. was seen in 1940 with a history of having been struck in the right eye by a comb at the age of three years which caused a small corneal laceration and small anterior synechias but no surgical repair was done. At the age of six years, a discission was done here. She was seen two years later with vision of counting fingers at three feet.

Case 9

P. In 1950, at the age of 13 years, was seen with a history of having been struck across both eyes by a stick at the age of four years, which caused a severe injury to the right eye necessitating enucleation for panophthalmitis three months later. The left eye had developed a traumatic cataract, as well as a corneal scar with adherent leukoma, and there was nystagmus. A discission was done but vision of light perception only remained unimproved.

Case 10

C. was seen in 1950 several months after having been struck in the right eye by an unknown object. A traumatic cataract was present and a discission done. Postoperative vision was light perception. He was seen several months later with no improvement of vision. A second discission was advised but has not been carried out.

Case 11

S. At the age of three years, the right eye was injured by the point of a scissors blade. The lens capsule was injured and the lens became opaque during the next year. She was treated with mydriatics throughout the year. In 1952, a discission was done. Postoperative vision was light perception. One year later a discission was again necessary. Two years after the last surgical procedure the vision was recorded as 20/200.

Case 12

H. In February, 1954, at the age of four years, suffered a dart puncture of the right cornea and lens. The lens became opaque and a discission was done in May, 1955. This did not provide a clear

TABLE 2

ANALYSIS OF 27 CASES OF TRAUMATIC CATARACT FROM SAN FRANCISCO (1937–1958)

Age (yr.)	No. Patients	Operations		Deviations	Vision	Comment
		1	2+			
1	3	2	1	1-ET	Nil	(I) Postop. endophthalmitis and enucleation (age 8 yr.)
					LP	(II) Linear ext. (3½ yr.). Discission (4 yr.)
					HM	(III) Discission (6 yr.)
2	1	1	—	XT	CF 1′	(I) Discission (4 yr.)
3	3	2	1	—	CF 6′	(I) Discission (9 yr.)
					CF 3′	(II) Discission (9 yr.)
					20/200	(III) Discission ('52 & '53)
4	3	1	1	—	5/200	(I) Age 7 incip. cat., optic atrophy
					—	(II) O.D., injury, enucleated
					LP	O.S., discission ×2 (13 yr.)
					HM	(III) Dart puncture '54, discission '54 & '55
5	1	1	—	—	HM	(I) Puncture wound, AC lavage spont. absorption
6	3	2	—	—	LP	(I) Arrow puncture, AC lavage spont. absorption (1940/1950—glaucoma. LP
					HM	(II) Slingshot, discission (1 yr.)
					LP	(III) Blow to eye, 6 mo. later discission
TOTAL 14						
7	2	1	1	—	5/200	(I) Knife Oct. 1943, suture linear ext. Nov. '43
					20/30	(II) 1949 discission, (Hawaii) cc & patch, '56 discission
8	3	1	1	—	HM	(I) Age 13, discission
				XT	20/400	(II) Stone, linear ext. '57–'58, discission (was 20/70)
				—	LP	(III) Nail puncture—FB.(head) spont. absorption
9	2	1	1	—	LP	(I) FB puncture, 1 yr. discission, 3 yr. discission
				—	20/20	(II) '46—cornea lac. sutured, '48—discission
10	2	2		—	2/200	(I) Linear ext. '39
					LP	(II) Slingshot Sept. '49, linear ext. Nov. '49
12	2	1	1	—	20/30	(I) '47 corneal lac sutures, '48 linear ext.
				—	LP	(II) Contusion '55, linear ext., 6 mo., glaucoma cyclodialysis & diathermy cyclodialysis
13	2	1	—	—	20/70	(I) Corneal lac., sutures, AC lavage, etc. Spont. absorption of the cataract
				—	20/30	(II) Stone hit LE, 9 mo. later intracap. ext.
TOTAL 13		?				

pupillary way so a Berens' scissor incision of the pupillary membrane was done in June, 1955. When last seen in March, 1958, the vision was hand movements at one foot.

CASE 13

W. at the age of one year was struck in the left eye by a metal Scotch tape holder. Six months after the injury the parents were informed that the child had a traumatic cataract. They claim they were advised to wait until the child reached the age of six years before surgery would be done. He was first seen here in 1956 at the age of nine years. A discission was done. At postoperative follow-up visits the vision was recorded as light perception. We have not seen him since.

CASE 14

L. was first seen here in 1957 with the history of having had an injury of unknown type to the right eye at the age of two years. He was now aged four years and presented with a traumatic cataract which

was treated by discission. When seen in 1958, the vision was counting fingers at six feet and he had a right exotropia. In 1959, the vision was counting fingers at one foot and the right exotropia measured 20 degrees.

Summary

University of California Medical Center

1. No patient had vision better than 20/200; most had counting fingers, hand movements, or light perception.

2. At least three patients developed deviations.

3. Nine patients underwent one operative procedure only, one patient had two operative procedures, two patients had cataracts which underwent spontaneous absorption, one patient did not have an operation.

4. One patient developed optic atrophy; one patient developed glaucoma.

5. One eye was lost after linear extraction and subsequent endophthalmitis (in 1937, pre-antibiotic).

Summary of 26 patients aged six years and under

(From both Montreal and San Francisco)

1. *Visual acuity.* Only one patient had vision of 20/30 or better with correction. This patient had intermittent occlusion and aphakic correction postoperatively until the injured eye's acuity had improved to 20/30+ (aged four and one-half years—E game). This is not an easy routine, but one which requires patience, effort and the complete cooperation of the child and parent.

2. *Deviation.* At least nine patients developed deviations, about equally divided between esotropia and exotropia. There were more deviations reported in the Montreal group than in the San Francisco group. This may be explained by the fact that the follow-up of cases was considerably longer in the Montreal series. In San Francisco many or the majority of cases were referred to out-of-town ophthalmologists after a short postoperative follow-up period.

3. *Operative procedures.* Nine patients underwent two or more operative procedures; four patients underwent three or more procedures. Three patients developed retinal detachment. Two of these had two or more procedures, the other a linear extraction. The incidence of multiple operative procedures was higher in the Montreal group as well as the incidence of retinal detachment (remembering of course that the follow-up period was shorter in San Francisco). One must also consider the experience of the San Francisco group with congenital cataract; Dr. Cordes[4] had warned many years ago that the incidence of retinal detachment was in direct proportion to the number of operative procedures performed on these eyes. In the same paper, Cordes draws attention to the increased incidence of vitreous traction bands after needlings. He expressed a preference for linear extraction.

One patient developed glaucoma and one eye was lost after an operative procedure in 1937 (pre-antibiotic era).

III. Patients over six years of age at time of injury

(13 cases—Montreal)

Case 1

K. L., at the age of 10 years, suffered a blow to the right eye which caused a hyphema. An opaque lens developed in two weeks. A discission was done at this time. The lens material absorbed satisfactorily without further complication. When seen two years postoperatively the vision was 20/70 (with aphakic correction).

Case 2

S. N., at the age of 11 years, was struck in the left eye by a BB shot which caused a small corneal laceration and ruptured the lens capsule. Six months later a discission was done and a good pupillary area was obtained. On postoperative follow-up visits the vision was hand movements only.

Case 3

W. B. In April, 1955, this 13-year-old boy was struck by an arrow which caused a minor corneal laceration and a contusion of the lens. By October, 1955, the lens was opaque and a discission was done. At the one-month postoperative follow-up visit the vision was 20/20 with correction. He has not been seen since.

CASE 4

E. P., aged 11 years, was struck by a stone in the left eye in 1940 and developed a cataract which was needled later that year elsewhere. Claimed vision after the operation was hand movements. He was first seen in our clinic in 1952 for correction of a left esotropia. Vision was hand movements only.

CASE 5

M. L. suffered an injury to her left eye in a fall at the age of 12 years. Six months later the lens was opaque. Discission was done. At postoperative follow-up visits vision was recorded as counting fingers at eight feet. No further examination was made.

CASE 6

G. T., at the age of 13 years, was struck by a stone hurled from a slingshot. The right eye developed a cataract which was needled within a year of the injury (1936). At postoperative visits vision was recorded as hand movements. Contacted by phone for this survey, I was informed that he "has been blind in the right eye for 20 years."

CASE 7

S. M. At the age of eight years a needle-pointed dart perforated the right cornea and injured the lens capsule. He was seen approximately one year after the injury at which time a discission was done. On postoperative visists his vision was hand movements. He has been lost to follow-up.

CASE 8

L. C. developed a traumatic cataract after a blow to the left eye at the age of nine years. A linear extraction was done with difficulty. A clear pupillary way was obtained. One year after the operation the vision was hand movements.

CASE 9

F. B. At the age of seven years, this boy suffered a perforating injury of his right cornea with tearing of the anterior lens capsule by a nail shot from a pop-gun. He was admitted to hospital immediately and the eye treated with mydriatics, occlusion and antiseptic drops (preantibiotic days). He was discharged after 10 days but had to be readmitted 10 days later because of elevated intraocular pressure. On this admission the anterior chamber was irrigated and considerable flocculent lens material was removed. Six days later the tension was again elevated and a second irrigation was done. At many postoperative visists, tension was normal. However, the best vision recorded was 4/60.

CASE 10

J. T. At the age of nine years the right eye was injured while playing with some tree branches. A traumatic cataract developed within several months and a discission was done. At postoperative follow-up visits vision was recorded as hand movements. He has not been seen since six weeks postoperative.

CASE 11

A. G. At the age of 11 years a small foreign body perforated the left cornea and lodged in the lens which became opaque within a two-week period. In July, 1945, a linear extraction was done with removal of the foreign body. A good pupillary opening was not obtained so a discission was done in October, 1945. Further discissions of the pupillary membrane were done in December, 1946, and July, 1947. He was not seen until April, 1953, when he appeared with a right exotropia and a detached retina, O.D. In June, 1953, a scleral buckling and surface diathermy procedure was done. In December, 1954, vision was light projection.

CASE 12

B. C. In 1945, at the age of eight years, a nail punctured the left eye while playing with sticks. A small corneal laceration and a tear in the anterior lens capsule were present. He was treated with mydriatics and bedrest. The lens underwent spontaneous absorption. When last seen in January, 1959, his vision was 20/20 with correction and he had exophoria.

CASE 13

G. F. At the age of 11 years a stone struck the left eye causing a corneal abrasaion. One month later the lens had become opaque. A discission was done at this time (June, 1954). In September, 1954, the pupillary membrane was needled. In October, 1958, vision was 20/20 with correction and left esotropia was present.

SUMMARY

1. In three cases vision was 20/20 with correction; one of these had no surgery, the lens undergoing spontaneous absorption. In one case vision with correction was 20/70; in the remainder, hand movements or counting fingers.

2. Four cases developed deviation, two esotropia and two exotropia.

3. Three cases underwent two procedures; two cases underwent three or more surgical procedures.

4. One case developed increased intraocular pressure after the lens injury and required emergency surgical relief on two occasions.

5. One case had four needlings, developed retinal detachment six years later and then had a scleral buckling procedure, with vision of light perception.

IV. Patients over six years of age at time of injury

(13 cases—University of California Medical Center)

Case 1

S., 1937. A firecracker explosion caused a corneal laceration, traumatic iritis and hyphema, and a traumatic cataract. The anterior chamber was irrigated, with removal of the blood clot and lens material. His postoperative course was satisfactory and when seen several years later the vision was 20/70 with correction, aged 13 years.

Case 2

M., 1934. A nail head broke when struck by a hammer. It perforated the cornea of the left eye and the lens. It was removed by the posterior route, using the giant magnet. The traumatic cataract underwent spontaneous absorption. Postoperatively there were several bouts of iritis. In 1938 when last seen, vision was light perception. This was four years after the original injury at the age of eight years.

Case 3

B., 1940. Was seen here with a traumatic cataract of the left eye after having injured the eye in a fall on a stick one year ago at the age of 11 years. Uneventful linear extraction was done. When seen nine years later, no fundal lesion could be found to explain the poor vision. Vision was 2/200 with correction.

Case 4

R., 1943. This seven-year-old boy was struck in the right eye by a knife which caused a corneal laceration with iris prolapse. The prolapsed iris was excised and the corneal wound closed immediately. One month later the traumatic cataract was treated by linear extraction. One year later the vision was 5/200.

Case 5

C., 1944. A nine-year-old boy suffered perforating injury of the left cornea by a piece of flying copper. The iris prolapse and corneal laceration were repaired immediately by excision and closure of the wound. An external filtering bleb formed near the irregular laceration site. In 1945, a linear extraction was planned but at surgery a discission was done instead. In 1948, the pupillary membrane was again treated by discission. In 1949, vision was light perception.

Case 6

L., aged 11 years. In 1944, at the age of nine years, this boy's right eye suffered a corneal laceration which was treated elsewhere by suturing. When seen here at the age of 11 years the traumatic cataract was treated by discission. Two years later corrected vision was 20/20.

Case 7

R., 1947. This 12-year-old boy fell on a tree stump causing a corneal laceration and hyphema. Within three months the lens became opaque. In August, 1948, a linear extraction was done. In December, 1948, corrected vision was 20/30.

Case 8

S., 1949. At the age of eight years, a foreign body perforated the right cornea and injured the lens. The foreign body was removed anteriorly elsewhere. When first seen here at the age of 13 years there was a traumatic cataract. A discission was done and the best vision recorded at postoperative follow-ups was light perception.

Case 9

L., 1949. In September, 1949, this 10-year-old patient was struck by an object hurled from a slingshot, causing a corneal laceration of the left eye. There was marked iritis and for a time it was feared the eye would be lost. In November, 1949, a linear extraction was done and at the same time a cilium was removed from the anterior chamber. He was last seen in June, 1959, with light perception but faulty projection. The fundus could not be seen. The prognosis was regarded as poor and although a discission was considered, this has not been done.

Case 10

H., 1955. This 12-year-old boy was injured in a firecracker accident in January, 1955. He had a corneal abrasion and in one month the lens had become opaque. In February, 1955, a linear extraction was done. In June, 1955, the intraocular pressure was markedly elevated and a cyclodialysis and cyclodiathermy were done. In December, 1955, the tension was again elevated and a second cyclodialysis was done. When last seen in June, 1956, the tension was normal and the vision was light perception.

Case 11

S., 1956. At the age of seven years, while in Hawaii, the patient injured the right eye by a stick shot from a slingshot. Several months after the injury he had an operation for cataract in Hawaii. The postoperative care there included intermittent occlusion of the normal eye and aphakic correction of the right eye. He was seen here at the age of 14 years when vision had diminished and it was thought advisable to incise the pupillary membrane. A discission was done in November, 1956. In January, 1957, corrected vision was 20/30. The clinic record mentions contact lens trial but this was not done.

Case 12

H., 1957. Five months prior to being seen here this 13-year-old boy was struck in the left eye by a stone. In June, 1957, an intracapsular extraction of the traumatic cataract was done. When seen in October, 1957, and November, 1958, corrected vision was 20/30.

CASE 13

M., 1957. An eight-year-old Negro boy injured the left eye in a fall with a stick several months prior to being seen here. A linear extraction was done in October, 1957. Vision in December, 1957, was 20/70. In December, 1958, the pupillary membrane required discission. Postoperatively the vision was 20/200. One year later in December, 1959, vision was 20/400 and there was optic atrophy. There was also left exotropia and left hypertropia.

SUMMARY

1. Four patients had vision of 20/20 or 20/30, one, 20/70−, the others hand movements, light perception or less.

2. Three patients developed deviations.

3. Four patients underwent two or more procedures. Two cataracts absorbed spontaneous, one patient having vision of 20/70, the other light perception. The other patients had one operative procedure.

4. One patient developed glaucoma and required repeated surgery.

5. One patient with 20/30 vision had intermittent patching and wore an aphakic correction at the age of seven years.

SUMMARY OF 26 PATIENTS OVER THE AGE OF SIX YEARS

(From both Montreal and San Francisco)

1. *Visual acuity.* Seven patients have corrected vision of 20/20 or 20/30; two patients have 20/70; the remainder, counting fingers, hand movements, or light perception. One of the patients with corrected vision of 20/30 was treated in Hawaii with postoperative intermittent occlusion and aphakic correction at the age of seven years.

2. *Deviation.* Seven patients developed deviations, four exotropias and three esotropias.

3. *Operative procedures.* Nine patients underwent two or more operative procedures. Two patients (one from each center) developed glaucoma postoperatively and required further surgery to control the glaucoma. One patient developed retinal detachment after four needlings. This occurred six years after the last needling.

DISCUSSION

1. VISUAL ACUITY

The aim is usually to obtain useful vision. This descriptive term has a wide range of variability. One might propose that useful vision be defined as that vision which would allow the afflicted individual to pursue whatever vocation and endeavors his interests and capacities may direct.

In a world which is demanding more in the way of good visual acuity to keep pace with ever faster ways of life, one must aim for something more than what has been acceptable in the past.

In the age group under six years when visual abilities are still developing, at least for the first four years, any insult to the eye interferes with the natural development of visual skill. If this natural development of vision is to continue, one must be prepared to deal with an anisometropia of approximately 10 prism diopters. This means intermittent occlusion of the normal eye and aphakic correction for the injured eye. This must be continued until good vision is obtained in the injured eye and then retained until after the age of six years at least by intermittent occlusion of the good eye unless the patient is one of the rare individuals who can tolerate such anisometropia.

In the age group over six years, there is somewhat more indication for obtaining a clear visual axis surgically because it seems that visual skills developed before the injury may be more readily recovered with refractive correction for the aphakia, in the absence of coincident damage to the remainder of the eye.

2. DEVIATION

Deviation occurs whether or not a clear pupillary area is obtained. The incidence is high in those cases with long-term follow-up, so that the figures given herein are quite likely much too conservative.

3. SURGERY

The results of surgery have been uni-

formly poor regardless of the procedure used. One could not emphatically recommend either discission or linear extraction on the basis of these results but the impression gained is that a linear extraction, when possible, may be more desirable. Intracapsular extraction has been done successfully in the older age group. No experience is recorded with zonulolytic agents but these may find their place in future years, although presently their use in childhood is not recommended. The textbooks state that surgery is a highly individual matter and usually add that these cases require "careful surgery." Perhaps it is best to conclude this section with a quotation which Dr. Cordes has used on occasion: "If you're not sure what to do, you had better not do it."

4. Complications

Two patients developed glaucoma shortly after the operative procedures on the lens. One of these required glaucoma surgery, the other was relieved by lavage of the anterior chamber. Four patients developed retinal detachments three to 20 years after the surgical procedures for cataract. Many of the patients were not seen for long-term follow-ups because they were referred to ophthalmologists nearer home after having surgery at the respective university centers. It is very possible and likely that, if all patients could be seen again, more complications, such as deviations, glaucoma, retinal detachments and so forth, would be found. On the other hand, one must consider that the seriously injured and complicated cases will more likely be referred to a university center and, because of this, the patients here reported may represent a somewhat selected group of cases. There has been no selection of cases at the university centers where this study was made.

It is interesting that McNabb in replying to Black's review stated that perhaps the improvement in contact lenses would do more toward restoring useful vision in these cases. One wonders how much has been accomplished in the 20-year interval since that time.

Finally, one can probably modify Baudry's statement made more than a half century ago, "every injury to the crystalline lens should be considered as a serious menace to the *existence* of the eye" to read, "every injury to the crystalline lens should be considered as a serious menace to *useful vision* in that eye."

Conclusion

The results of treatment of 52 cases of traumatic cataract in children seen at two widely separated medical centers are presented. It is interesting that the results and the number of cases seen over a similar period of time at the respective centers are so similar. The visual acuity obtained is uniformly poor, only one patient under the age of six years had vision of 20/30 and seven patients over this age had 20/30 or better. Suggestions are made regarding the management of these cases and some of the complications of surgery are listed. Before planning surgery more consideration must be given to assessing the visual potential of the eye and the surgical technique to be used and to planning the rehabilitation of an eye in which the visual optics have been radically changed.

The Wilmer Institute,
The Johns Hopkins Hospital (5).

Acknowledgment

I wish to thank Dr. B. Alexander, chief of ophthalmology, Montreal General Hospital, Dr. S. T. Adams, chief ophthalmologist, Montreal Children's Hospital, and Dr. M. J. Hogan, chief of ophthalmology, University of California Medical Center, San Francisco, for making their records available, and Dr. F. C. Cordes, professor emeritus of ophthalmology, University of California Medical Center, San Francisco, for his constructive criticism and suggestions.

References

1. Juler: Amblyopia from disuse: Visual acuity after traumatic cataract in children. Tr. Ophth. Soc. U. Kingdom, **41**:129, 1921.
2. Clapp: Southern M. J., **31**:552, 1938.

3. Black and McNabb: Treatment of traumatic cataract. Tr. Ophth. Soc. U. Kingdom, **62**:207-213, 1943.
4. Cordes, F. C.: Failure in congenital cataract surgery: A study of fifty-six enucleated eyes. Am. J. Ophth., **43**:1 (Jan.) 1957.
5. ———: Management and surgery of traumatic cataract. Southwest M. J., **20**:290, 1936.
6. Haik, G. M.: Symposium on Diseases and Surgery of the Lens. St. Louis, Mosby, 1957.
7. Kirby, D.: Surgery of Cataract. Philadelphia, Lippincott, 1950.
8. Castroviejo, R.: Trends in cataract surgery. In Sorsby, A.: Modern Trends in Ophthalmology. New York, Hoeber, 1947. Vol. II. pp. 449-468.
9. Baudry, S.: Injuries to the Eye in Their Medico-legal Aspect. Philadelphia, Davis, 1900.

THE OCCURRENCE OF CONGENITAL KERATOCONUS POSTICUS CIRCUMSCRIPTUS*

In two siblings presenting a previously unrecognized syndrome

William P. Haney, M.D., and Harold F. Falls, M.D.
Ann Arbor, Michigan

Keratoconus posticus circumscriptus is a rare congenital aberration of development of the cornea. In a paper by Butler,[1] Stallard first described this condition as follows; "It is best described as the appearance one might expect if into the posterior surface of a plastic cornea one had excavated a subsidiary small basin-like depression by pressing into it a marble of much smaller curvature than that of the corneal surface itself." In other words, a sharply localized increase in curvature of the posterior corneal surface constitutes the entity (fig. 1). A gray opalescent alteration of the involved portion of the cornea is visualized with the biomicroscope. This aberration is usually, but not always, axial in position. It may or may not interfere with visual acuity, depending upon its position, extent, and the density of corneal scarring.

Jacobs[2] summarized the world literature in 1957. He pointed out the rarity of this disorder. There were seven reported cases of keratoconus posticus circumscriptus at the time of his publication. He added three cases of his own and four more cases which had occurred in previously diseased or traumatized eyes. We were not able to find, in the world ophthalmic literature, a report of keratoconus posticus circumscriptus as a component of a systemic syndrome. It is the intent of this paper to present an account of keratoconus posticus circumscriptus occurring in two siblings and furthermore, to suggest that, at least in this family, the entity is associated with a previously unrecognized syndrome.

At the present time 17 cases[1-14] are to be found in the world ophthalmic literature. Of these cases, seven have occurred in previously diseased or traumatized eyes. Only six times has this condition been observed in both eyes of one person. Eccentric lesions account for eight reported cases. In these the axial cornea was spared. The lesion has occurred in two members of the same family only once previously.[2]

Since the cases constituting our report were in siblings, a complete pedigree of the family was obtained. The parents denied any possibility of consanguinity. In evaluating the pedigree, no other affected members were uncovered from the information given by the parents. The inheritance pattern is difficult to determine, but the disease seems to be inherited as an autosomal dominant with poor penetrance although recessive inheritance cannot be excluded (fig. 2).

The two cases presented here were recently examined at the University Hospital

* From the Department of Ophthalmic Surgery, University Hospital.

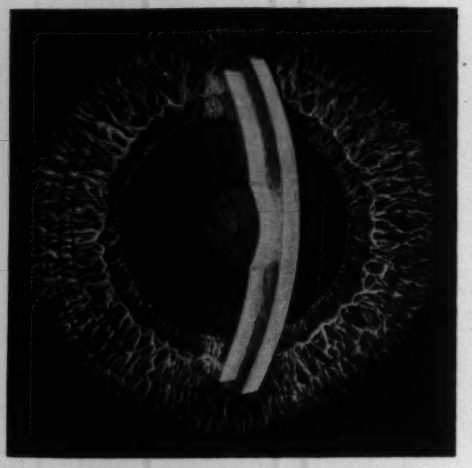


Fig. 1 (Haney and Falls). Artist's conception of the defect in the posterior surface of the cornea, illustrating the circumscribed nature of the defect and the opacity in the involved portion of the corneal stroma.

and are important in the following respects: First, we believe this to be the second example of a familial link in this disorder. Second, we feel that the evidence suggests that this disorder is a manifestation of a genetic defect. Third, the associated anomalies may be of interest as a classifiable syndrome.

Case reports

Case 1

A 17-year-old white youth entered the Ophthalmology Out-patient Service of the University Hospital on August 5, 1960, stating that his eyesight was not good enough to pass the Ohio State Driver's License Test. His eyesight had been poor since birth. At four weeks of age the boy was examined by Drs. Fralick and Falls of the University of Michigan Department of Ophthalmology. They noted a distinct grayish-white infiltration extending deeply into the axial cornea. A diagnosis of corneal macula, O.U., was made and it was felt that an optical iridectomy might be of value.

The patient had received no treatment except glasses until the present examination. The visual acuity

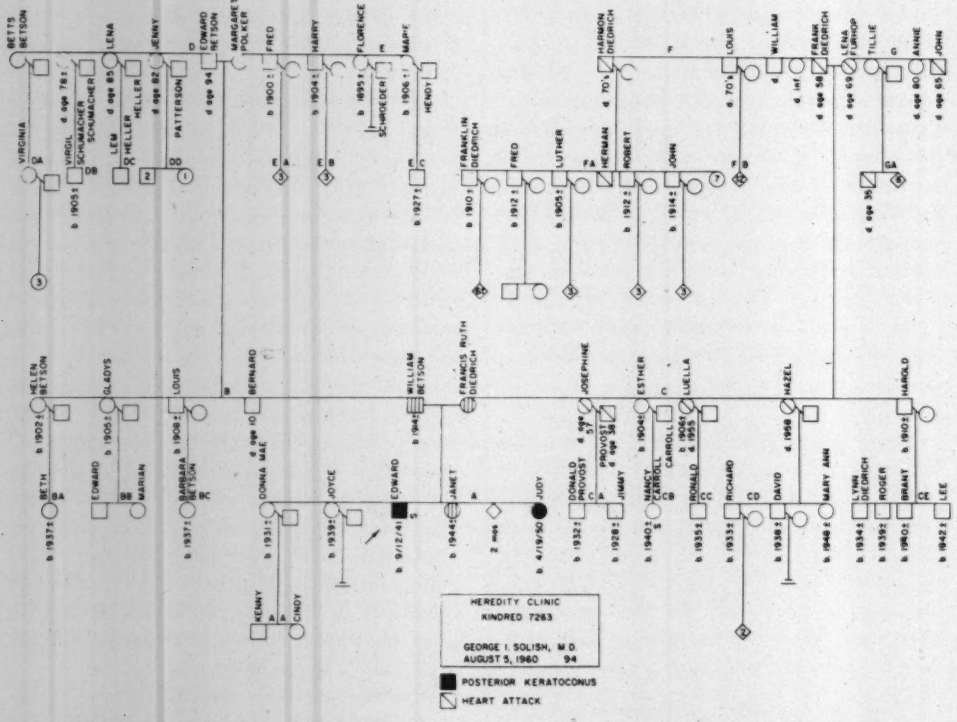


Fig. 2 (Haney and Falls). A complete pedigree of the family as obtained by the University of Michigan Heredity Clinic. Only the two members described in this paper appeared to be involved.

was 20/100, O.D., and 20/200, O.S. He read J7, O.S., and J0, O.D. The distance between the inner canthi was 36 mm. and the bridge of the nose was flat. The eyes were straight in the primary position and the extraocular movements were full although wide divergence occurred under cover. There was no fusion and left eye suppression was demonstrated on the Worth four-dot test. Axial corneal nebulae were present, O.U. Ophthalmoscopy revealed a fundus distorted by myopic astigmatism, O.U. The central retinal vessels swept from the disc nasally and fanned out temporally. Under the slitlamp beam there was an obvious depression in the posterior surface of each cornea, "as though a marble had been pushed into it." At the edges of the depression there were three or four chocolate-colored endothelial precipitates. The axial cornea at the base of the depression was nebulous. There was no evidence of inflammatory reaction apparent in the anterior chamber. Iris and lens appeared to be normal. Keratometer readings, O.D., were 43.37 horizontally and 46.10 vertically. Retinoscopy revealed that a —9.0D. sph. and plano cylinder gave a visual acuity of 20/100, O.D., and a —8.0D. sph. ⌒ —6.0D. cyl. ax. 90° gave a visual acuity of 20/200, O.S. Correction of the refractive error with contact lenses did not improve the visual acuity.

A physical examination was performed. The boy was five ft., one in. tall and weighed 120 pounds. His arms were 55 cm. long and the circumference of the neck was 39 cm. There was a mild systolic basal heart murmur, fairly marked brachydactyly, and a shuffling, stiff-legged gait. The limbs appeared short and stubby, but no osseous or muscular defect could be found (fig. 3).

The chest X-ray film and routine laboratory work were normal. Skull X-ray films were also normal. An oral examination complete with full mouth X-ray films revealed no abnormality of the jaws or teeth. Buccal smears revealed normal male cytologic sexual pattern.

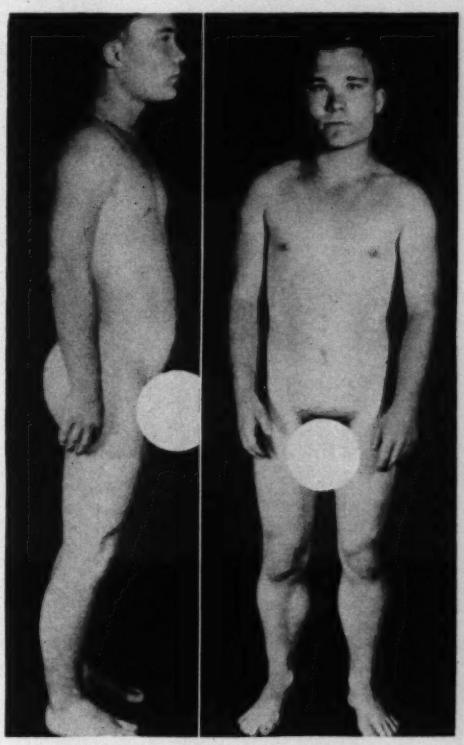


Fig. 3 (Haney and Falls). *Case 1.* These photographs illustrate the underdevelopment of the root of the nose, the hypertelorism, broad neck, short stubby arms and barrel chest, typical of both siblings.

CASE 2

The 10-year-old white girl, a sibling of the patient in Case 1 presented herself at the Ophthalmology Clinic of University Hospital with no ocular complaints. The vision in the right eye had been poor since birth but no treatment had been given.

The visual acuity without correction was counts fingers, O.D., and 20/70, O.S. The distance between the inner canthi was 34 mm. and the bridge of the nose was broad and flat. The eyes were straight in the primary position and the extraocular movements were full. The PCB was remote. There was no fusion capacity, and the right eye was suppressed on the four dot test. An axial corneal nebula was present, O.D. The fundus was similar to the older sibling's. The central retinal vessels swept nasally from the center of the disc and fanned out temporally. The slitlamp beam revealed an axial depression in the endothelial surface of the right cornea, exactly similar to the corneal lesions in the older brother. At the edges of the depression were three to four chocolate-colored endothelial deposits. The axial corneal stroma was cloudy. The anterior chamber was clear. Iris and lens appeared normal. Keratometer readings, O.D., were 42.25 horizontally and 46.75 vertically. Retinoscopy revealed a —1.0D. sph. ⌒ + 3.0D. cyl. ax. 75°. This correction did not improve the vision of the right eye. Retinoscopy of the left eye revealed a marked scissorslike reflex, similar to the reflex in the right eye. A —0.5D. sph. ⌒ +0.5D. cyl. ax. 90° gave a visual acuity of 20/70, O.S.

The child was under treatment by a local physician for a hypothyroid condition and was now taking one-half tablet of thyroid extract per day. She was mentally retarded and had developed a dependent personality.

A physical examination was performed. The girl was four ft., one in. tall and weighed 65 lb. (fig. 4). The circumference of the head was 51.2 cm., of the neck 35 cm., and a marked webbing of the neck was noted. Her arms were 46 cm. long. The head was large with wide-spaced eyes. The nose was flat and broad. The hands were broad and the fingers were short. She had a stiff-legged gait and the feet were abducted.

Skull X-ray films were normal. Complete oral examination with full mouth X-ray films revealed a

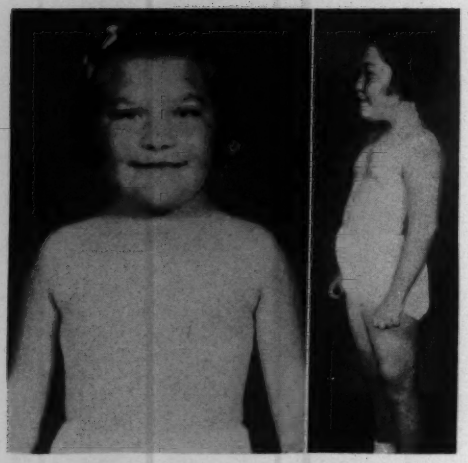


Fig. 4 (Haney and Falls). *Case 2.* This girl shows fairly marked webbing of the neck and a prognathic malocclusion along with aberrations noted in her sibling, Case 1.

prognathic malocclusion with possible underdevelopment of the maxilla. Buccal smears revealed a female cytologic pattern.

Discussion

That keratoconus posticus circumscriptus is a rare lesion cannot be doubted. These appear to be the first cases to have been observed in this department within recent memory. In reviewing the reported cases, several aspects regarding this disease become apparent. Trauma and ocular disease may cause a circumscribed defect in the posterior surface of the cornea. This acquired defect is not necessarily axial, nor is it precise in curvature. It may or may not interfere with vision. This represents a different entity from that which is described in this paper and should be differentiated from it. The congenital circumscriptus lesion has been attributed, by some, to delayed separation of the lens from the corneal endothelium in the formation of the anterior chamber. Greene[10] observed anterior lenticular opacities directly in line with the corneal lesion and offered this as evidence of an abnormal separation. No such lenticular opacities were observed in our cases. Pigmented deposits about the lesion were observed by us and have been observed before.[6] These deposits resemble uveal pigment and are aligned in concentric fashion about the edges of the lesion. It seems quite likely that these pigment deposits were derived from the pupillary border of the iris.

DeRosa,[13] on the other hand, feels that underdevelopment on the central endothelium provides an obstacle to the migration and to the normal disposition of the mesodermic cells of the corresponding area. As a consequence, there is a standstill of development of the corneal parenchyma in the area involved. He, therefore, feels that the whole malformation should be connected to an incomplete constitution of the posterior endothelial lamina.

Two facts observed in our cases offer strong evidence in favor of a congenital genetic defect leading to keratoconus posticus circumscriptus. The first is the appearance of nebulae at an early age and a negative maternal history for exposure or affection with the acute exanthemas, and the second, and most important, is the occurrence of the identical defect in two siblings.

Corneal nebulae have been observed in almost every case of keratoconus posticus and appear to be an almost constant finding. These nebulae are present at the base of the lesion where the cornea is thinnest. Case 1 possessed these nebulae at a very early age as evidenced by the examination of his eyes at the age of eight weeks. It appears quite likely, therefore, that keratoconus posticus circumscriptus was present since birth and could hardly have been caused by postnatal trauma or disease. Although we would expect the aberration to be bilateral in Case 2, it was not. She did, however, manifest an unusual scissorlike reflex in the uninvolved eye on retinoscopy. This reflex was postulated by Butler[1] in his original paper to be a manifestation of the aberration.

More interesting is the fact that the identical defect occurred in two siblings. It would be difficult to conceive of any trauma or dis-

ease causing an identical arrest of development either pre- or postnatally in these two children. It, therefore, appears that this corneal lesion is a congenital genetic defect. The complete pedigree of the family failed to elicit the occurrence of any ocular disease of any importance in the relatives. We feel, therefore, that the interpretation of the Heredity Clinic at the University of Michigan is as correct as possible in the light of the available evidence. That is, the disease seems to be inherited as an autosomal dominant with poor penetrance although recessive inheritance cannot be excluded. To support this hypothesis further Jacobs[2] reported the occurrence of keratoconus posticus in a father and son.

During the course of the examination much curiosity was aroused because of the unusual and remarkable similarity of the two children (figs. 3 and 4). Their wide-set eyes with upward displacement of the lateral canthi, broad flat noses, thick necks, barrel chests, and stubby limbs and fingers, suggested a congenital constitutional syndrome. No mention of these associated features was found in the literature. The following characteristics may indeed be representative of a new and hitherto undescribed syndrome:

1. Keratoconus posticus circumscriptus.
2. Corneal nebulae.
3. Myopic astigmatism.
4. Corneal endothelial precipitates.
5. Hyperteleorism—mild.
6. Poor development of the bridge of the nose
7. Upward displacement of the lateral canthi
8. Brachydactyly
9. Webbed or bull neck (pterygium colli)
10. Mental retardation
11. Stunted growth

Further study of the syndrome is in progress.

Conclusion

Two cases of the rare corneal lesion, keratoconus circumscriptus, were presented. Evidence was presented to support the hypothesis that this lesion represents a genetic abnormality. Associated anomalies in these two siblings are described which are postulated as comprising a previously undescribed syndrome.

University Hospital.

References

1. Butler, T. H.: Keratoconus posticus. Tr. Ophth. Soc. U. Kingdom, **50**:551-556, 1930.
2. Jacobs, H. B.: Posterior conical cornea. Brit. J Ophth., **41**:31-39, 1957.
3. ———: Traumatic keratoconus posticus. Brit. J. Ophth., **41**:40-41, 1957.
4. Goldsmith, A. J. B.: Bilateral circumscribed posterior conical cornea. Tr. Ophth. Soc. U. Kingdom, **63**:180-181, 1943.
5. Leopold, I. H.: Keratoconus posticus circumscriptus. Arch. Ophth., **30**:732-734, 1943.
6. Ingram, H. V.: Keratoconus posticus. Tr. Ophth. Soc. U. Kingdom, **56**:263-264, 1936.
7. Butler, T. H.: Discussion on the "Rarer forms of keratitis." Tr. Ophth. Soc. U. Kingdom, **57**:33-36, 1937.
8. ———: Two rare corneal conditions. Brit. J. Ophth., **16**:30-35, 1932.
9. Wise, G.: Keratoconus posticus circumscriptus. Am. J. Ophth., **27**:1406-1408, 1944.
10. Greene, P. B.: Keratoconus posticus circumscriptus. Arch. Ophth., **91**:432-433, 1945.
11. Duke-Elder, S.: Textbook of Ophthalmology. St. Louis, Mosby, 1938, v. 2, p. 1281.
12. Berliner, M. L.: Biomicroscopy of the Eye. New York, Hoeber, 1949, v. 1, pp. 297, 363.
13. DeRosa, C.: Su di un caso di cheratocono posteriore. Arch. Ottal., **63**:445-455, 1959.
14. Guimares, W.: Argu. Bras. Oftal., **16**:209, 1953.

EXPERIMENTAL HYPHEMA IN RABBITS*

III. Effect of iridectomy, iridencleisis and temporary elevation in intraocular pressure on the rate of absorption

Robert M. Sinskey, M.D., and Alice R. Krichesky, A.B.
Los Angeles, California

In previous studies it has been shown that red blood cells leave the anterior chamber of the eye intact in large numbers; mydriatics and miotics have no effect on the rate of absorption of these red blood cells from the anterior chamber;[3] and Diamox, given systemically, markedly increases the rate of absorption over control groups but has a critical dosage range.[4] This phase of the study will show the effect of iridectomy, iridencleisis and temporary elevation in intraocular pressure on the rate of absorption of hyphemas. All these conditions .. ve clinical analogies.

Methods and Materials

Animals and techniques previously established[2] were used for labeling of red blood cells, injection into the anterior chamber and the counting of peripheral blood specimens.†

Obtaining and treatment of statistical data

The counts per minute per 1.0 cc. of the tagged blood injected into the anterior chamber were obtained for each experiment and known as the standard. The counts per minute for each peripheral blood specimen were reduced to a percent of its standard and designated as the percent absorption of the hyphema at the indicated intervals. The blood dilution factor was considered to be a constant since it fell within acceptable statistical limits of variability. The percent absorption figures for all animals in each series at each time interval were subjected to the rank sum and T test. The percent difference of absorption between the treated animals and the controls was calculated. The above statistical analysis of the data was done by the Department of Biostatistics, University of California Los Angeles Medical Center, under the supervision of Wilfrid J. Dixon, Ph.D.

1. Iridectomy

After anesthetization of each rabbit with intrapleural Nembutal (Abbott), 30 mg. per kg., the anterior chamber of one eye was entered at the limbus of the cornea with a keratome. The iris was grasped with iris forceps, pulled through the incision and a large complete iridectomy performed. The incision was closed with a 6-0 silk suture. Eserine ointment, 0.25 percent (Abbott), and Neosporin ointment (Burroughs and Welcome) were instilled in the eye after surgery. Two weeks were allowed for recovery. Only those animals showing an uncomplicated complete iridectomy were used for the study (fig. 1). The iridectomized eye with a hyphema 30 minutes after its induction can be seen in Figure 2.

* From the Division of Ophthalmology, Department of Surgery, University of California Medical Center. This investigation was supported by grant-in-aid B-929 from the National Institutes of Neurological Diseases and Blindness, United States Public Health Service.

† Adult, albino rabbits were used throughout the study. Only one eye of each rabbit was subjected to experimental study. Whole rabbit blood, in acid citrate dextrose solution and heparin was incubated at 80°F. plus or minus 2°F. for 90 plus minutes with 200 μc. of Cr51 per 3.5 cc. of whole blood. After washing at least three times with Ringer's solution the uptake of Cr51 in the cells was fixed by the addition of six plus or minus mg. of ascorbic acid per 3.5 cc. of whole blood. Tagged cells, 0.05 cc., were injected into the anterior chamber of the rabbit's eye after the removal of 0.05 cc. aqueous humor, using a 27-gauge, one-inch needle. Peripheral blood specimens were obtained by bleeding from an ear vein at specified time intervals after the injection of the tagged cells into the anterior chamber. All blood specimens were counted in a deep well scintillation counter.

Duration of Experiment. Experimental observations were made over a period of seven hours. Peripheral blood specimens for counting were obtained at three, five, and seven hours. Animals were killed and disposed of according to radiation safety regulations.

2. IRIDENCLEISIS

After anesthetization of each rabbit with intravenous Nembutal, 30 mg. per kg., a large conjunctival flap was elevated at the 12-o'clock position. An ab externa incision was made and enlarged with Aebli scissors. The iris was grasped, cut radially from the ciliary margin to the sphincter, and one pillar was pulled into the incision. The conjunctiva was closed securely with a running 6-0 plain catgut suture. Four weeks were allowed for recovery. Only those animals showing an uncomplicated iridencleisis were used for the study (fig. 3).

Duration of experiment. Experimental observations were made over a period of 48 hours. Specimens for counting were obtained at three, five and seven hours after induction of the hyphema. Since there were indications of significant changes at the end of seven hours, samples were counted at 24 and 48 hours. Animals were killed routinely at conclusion of 48 hours.

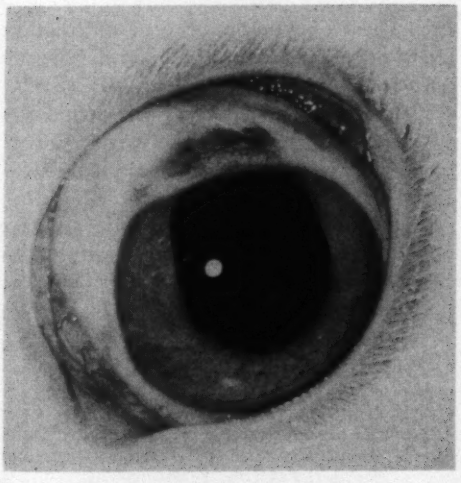


Fig. 1 (Sinskey and Krichesky). Iridectomized rabbit eye.

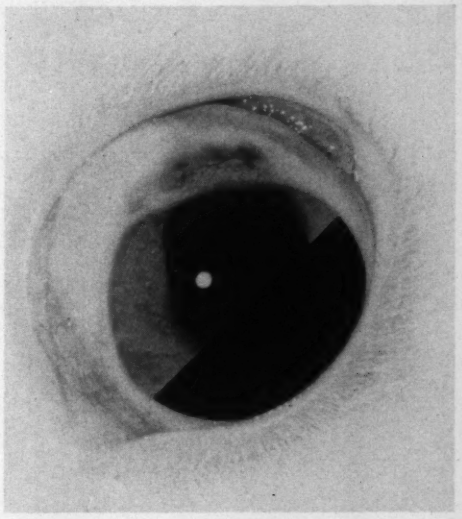


Fig 2 (Sinskey and Krichesky). Iridectomized rabbit eye with hyphema 30 minutes after its induction.

3. TEMPORARY INCREASE IN INTRAOCULAR PRESSURE

The intraocular pressure was increased temporarily by injecting 0.05 cc. of tagged red blood cells into the anterior chamber without removing an equivalent amount of aqueous first. The control group had 0.05 cc. of aqueous removed before injecting the tagged red blood cells.

Duration of experiment. Experimental observations were made over a period of 48 hours. Peripheral blood specimens for counting were obtained at three, five and seven hours after induction of the hyphema. Since the data at the end of seven hours were questionable in regards to significance, samples were counted at 24 and 48 hours. Animals were killed routinely at conclusion of 48 hours.

RESULTS

1. IRIDECTOMY

The number of animals iridectomized was 48; controls 48. Statistically there is no sig-

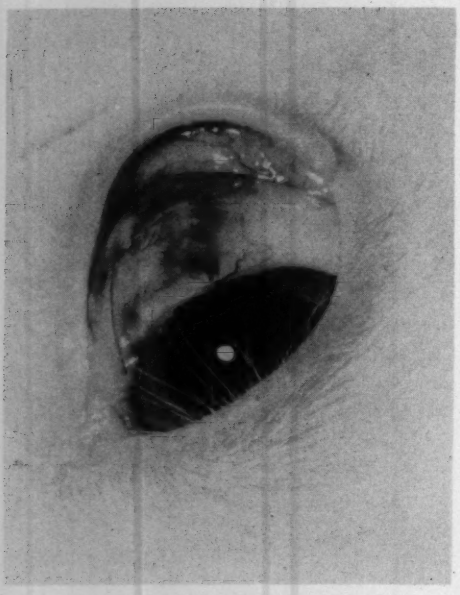


Fig. 3 (Sinskey and Krichesky). Iridencleisis in rabbit eye.

nificant difference in the absorption of blood from the anterior chamber between the treated animals and the controls.

2. Iridencleisis

The number of animals undergoing iridencleisis was 43; controls, 40. Statistically the iridencleisis group showed the following: from seven to 24 hours after the injection of the red blood cells—31.58 percent faster rate of absorption than the control group; 24 to 48 hours—30.03 percent faster rate of absorption.

3. Temporary increase in intraocular pressure

The number of animals with the aqueous intact, 42; controls, 42. Statistically there was no significant difference in the rate of absorption between the treated animals and the controls.

Discussion and Conclusions

Thomas[5] and Maynard[1] attempted to show by histologic techniques that the red blood cells were absorbed through the crypts of the iris. According to our techniques, removal of approximately one fifth of the iris does not alter the rate of absorption of red blood cells from the anterior chamber of the rabbit's eye. This would indicate that, although histologically red blood cells may be seen in the crypts of the iris, this is not a significant route of escape for them.

Iridencleisis increases the rate of absorption of red blood cells from the anterior chamber. This probably occurs by by-passing the normal outflow system, that is, trabeculae, Schlemm's canal, aqueous venous plexus, by the formation of a filtering bleb. The cells probably go directly from the anterior chamber to the subconjunctival vessels at a very rapid rate.

The transient increase in intraocular pressure produced by the introduction of 0.05 cc. tagged red cells does not noticeably alter the rate of absorption of these cells. Apparently the rise in pressure is so evanescent by this technique that no measurable increase of the hyphema absorption can be noted.

Summary

1. The removal of one fifth of the iris does not affect the rate of absorption of red blood cells from the anterior chamber of the rabbit eye. Therefore, one must conclude that no appreciable numbers of red blood cells are absorbed through the crypts of the iris.

2. Iridencleisis results in a more rapid rate of absorption of red blood cells from the anterior chamber of the rabbit's eye than in the intact eye.

3. A transient rise in intraocular pressure has no appreciable effect on the absorption of blood from the anterior chamber. This does not imply that prolonged rise in intraocular pressure has no effect.

School of Medicine (24).

Acknowledgments

We wish to express our appreciation to Dr. Bradley R. Straatsma for support during the course of this work; to Dr. Wilfrid J. Dixon, biostatistician, for his supervision of the statistical analysis of experimental data; to Mr. Robert J. Hendrickson for assistance in the laboratory.

References

1. Maynard, R. B.: Experimental hemorrhage in rabbits: First report. Tr. Ophth. Soc. Australia, **1**: 32, 1939.
2. Sinskey, R. M.: Experimental hyphema in rabbits. Am. J. Ophth., **43**:292, 1957.
3. Sinskey, R. M., and Krichesky, A. R.: Experimental hyphema in rabbits: I. The effect of mydriatics and miotics on the rate of absorption. Am. J. Ophth., **48**:215, 1959.
4. ———: Experimental hyphema in rabbits: II. The effect of acetazolamide (Diamox) on the rate of absorption. Am. J. Ophth., in press.
5. Thomas, F.: Research on the resorption of experimental hyphemia. Arch. ophtal., Paris, **46**:272, 1929.

OCULAR REACTIONS TO PLASTIC MATERIALS (POLYETHYLENE AND TEFLON)

K. E. Schirmer, M.D., and S. S. Raphael, M.B.

Montreal, Quebec

In ocular surgery polyethylene is frequently used, especially in detachment surgery,[1,2] since it excites relatively little reaction in the surrounding tissues. The literature contains some criticism to this material[3,4] and, therefore, new plastic materials seem always an appreciated addition,[5] in the hope of preventing any possible tissue response to a plastic foreign body. One of the most advocated plastic materials is Teflon, which has been used extensively in general surgery, especially in surgery of the vascular system.

Teflon provokes remarkably little reaction,[6] and may be regarded as inert a foreign body as ever can be hoped to become available. The chemical properties of this plastic material are such that no chemical reaction is to be expected under any pH after the plastic material has been implanted into the tissues. It is understood, however, that no plastic material can be fully inert, as a slight inherent rigidity in any foreign material will cause unnatural pressure and minimal trauma to the surrounding tissue which, in itself, may be sufficient to cause an ensuing reaction.

Considering the relative rigidity of polyethylene, Teflon's pliability is, at first sight, a great advantage, since this would reduce the possibility of its acting as a physical foreign body. The comparison of Teflon with the much used polyethylene seems an interesting experiment in evaluating intra- and extraocular tissue tolerance. The relative merits of the two plastics could, in our opinion, be best evaluated by applying both materials intra- and extraocularly in the same animal, recording the postoperative tissue reactions and the histologic picture several months after surgery.

Methods

The left and right eyes of 10 rabbits were operated at the same time under anesthesia with pentothal and ether. The conjunctiva was incised approximately five mm. behind the limbus at the 12-o'clock position, and dissected down to the limbus. A keratome incision was performed at this site, entering the anterior chamber. Through this opening a plastic wick of polyethylene 0.0015 mm. was inserted in each left eye, and a plastic wick of Teflon 0.5 mm. in each right eye. The pieces of plastic were approximately 5.0 by 3.0 mm. size. The conjunctiva was closed with one or two 4-0 plain catgut sutures. Chloromycetin succinate was injected under the conjunctiva at the 6-o'clock position, in a concentration of 100 mg. per cc., so as to achieve a better asepsis.

The animals were checked four months postoperatively and, after that period, were killed by an overdose of pentothal intravenously. Before that, the eyes were photographed and, after death, both eyes were

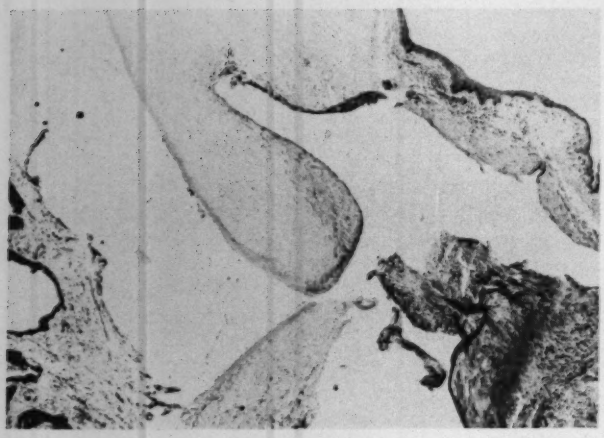


Fig. 1 (Schirmer and Raphael). Section through the drainage channel at the limbus and the filtering bleb. The filtering channel was kept open by a polyethylene wick that cannot be demonstrated in the section but was present in the paraffin block. Note the endothelial lining of the anterior lip of the wound and on the conjunctival side of the filtering scar. The endothelium is better visualized with the large magnification. (Hemotoxylin-eosin, ×120.)

enucleated. The position of the surgical scar in a paraffin-embedded specimen was marked with black silk to insure easy localization of the site of operation. The sections were stained with hematoxylin-eosin.

Results

Postoperatively, there was little reddening and tissue reaction. The operated eyes were treated with atropine and hydrocortisone eye ointment, as well as Chloromycetin locally. This treatment was stopped approximately 10 days after surgery had been performed. In only one case could infection be recorded, which was diagnosed as panophthalmitis, starting approximately 14 days after surgery. Despite treatment, the condition flared up intermittently, and persisted until the animal was killed with the rest. Except for one more eye that showed extrusion of plastic foreign bodies within the first month after surgery, with ensuing iris prolapse, there was no ciliary flush or conjunctival redness observed four months after surgery.

The description of tissue reaction in the subconjunctival space and anterior chamber, as well as the limbal wound, seemed most pertinent and indicative because of the imme-

TABLE 1*

Results of study

	O.S.				O.D.			
	Polyethelene				Teflon			
	Macro		Micro		Macro		Micro	
1	−	−	−	−	−	−	+	−
2	−	−	+	−	−	−	−	−
3	++X	+	++	++	−	++D	+	++D
4	−	−	+	−	−	−	−	−
5	−B	+	−	−	+++B	+++	+++	+++
6	−	−	−	−	−B	−	−	+
7	+B	−	+	−	−B	−B	−	−
8	+	−	+	−	+	++	+	++
9	++	++	++	++D	−B	−	−	−
10	+	++	+	++D	−	++	+	+

* Macroscopic and microscopic findings are correlated, as were intra- and extraocular findings. A dash indicates no reaction, plus, slight, double plus, moderate, and triple plus, marked reaction. B stands for bleb, indicating the macroscopic presence of a filtering scar, D stands for fibrous downgrowth, and X for extrusion of plastic material and iris prolapse.

diate vicinity to the inserted plastic materials. A tabulation of our findings in the 10 rabbits is shown in Table 1. We have made it a practice to consider the slides as an analogue computer would, marking them 1+, 2+, or 3+, depending on the tissue reaction or abnormality in the slide under study. Although attempts to assess pathologic reactions in a slide quantitatively in this manner are crude, it nevertheless seems a helpful gauge.

Discussion

Considering all findings as outlined in Table 1, we must be aware that several factors contribute to this result. None of them can be weighed with complete accuracy in considering the part they take in eliciting the pathologic reaction. Among the factors are surgical trauma and infection, as well as the reaction to the plastic foreign body. As, however, conditions seem comparable in both groups within the framework of the experiment, these variables should be sufficiently equally distributed.

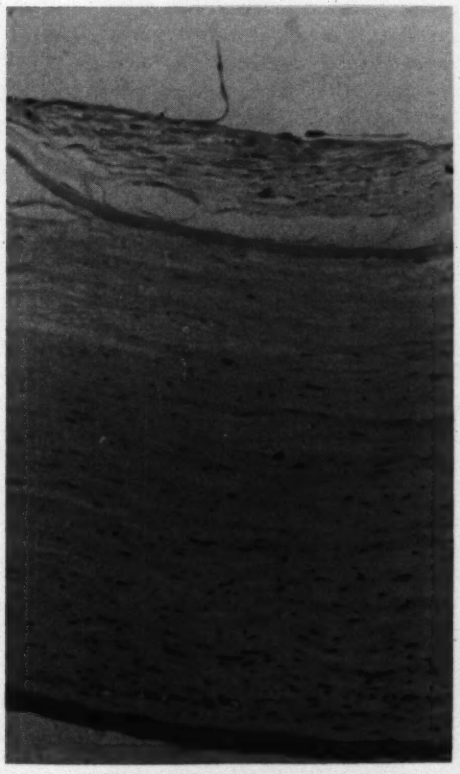


Fig. 2 (Schirmer and Raphael). Fibrous downgrowth along the back surface of the cornea. (Hematoxylin-eosin, ×100.)

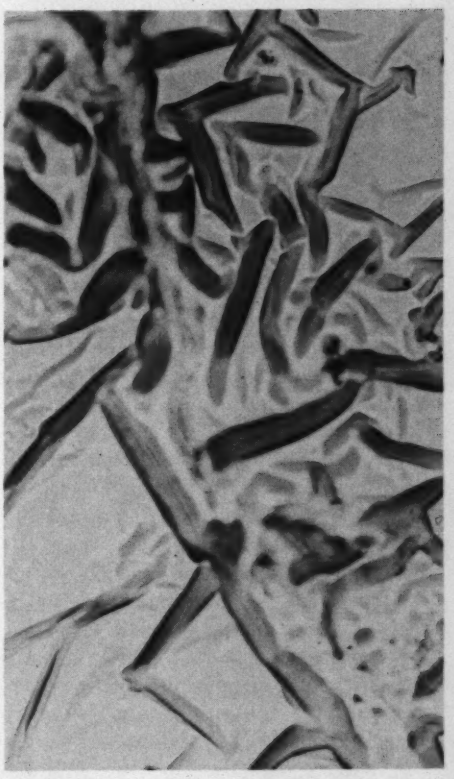


Fig. 3 (Schirmer and Raphael). Folds and wrinkles in the Teflon sheet as observed under the microscope. (×180).

In influencing the final result, the only variable remains the difference in plastic materials. Our aim is, therefore, to compare polyethylene and Teflon, rather than to assess its absolute value for ocular surgery in general. Considering our results, we cannot help but be favorably impressed by the lack of tissue reactions, having in mind the difficulty of operating on animals with perfect asepsis.

Reviewing our tabulated findings, we con-

clude that our point score system shows numeric values of approximately the same magnitude. Evaluating the findings statistically, we cannot see a great deal of difference between the reactions elicited by polyethylene and Teflon. One could argue that most of the reactions as seen under Teflon were due to Case 5, which was actually a case of postoperative panophthalmitis. If we were to eliminate this case in our tabulations, we arrive at no significant difference in intraocular reaction between the two plastics.

The relative absence of postoperative infections, except for one case, and the fast clearance of postoperative reactions, may in part be attributed to the use of Chloromycetin succinate, which was injected subconjunctivally immediately after surgery. The site of injection showed no sign of any reaction or swelling.

The relative absence of reactions to the plastic materials brings to mind the few instances in which plastic tubes of small caliber were used for glaucoma surgery to drain aqueous from the angle of the anterior chamber toward the episcleral tissue. These experiments have been described and several surgeons have used the procedure in a few cases. The sloughing of the plastic material through the conjunctiva seems to have been one major drawback in this procedure.

Considering the relative rigidity of polyethylene tubes, and the sharp edges where the tubes had been cut, it is not surprising that pressure necrosis and sloughing through the conjunctiva, with extrusion of the plastic foreign body, occurred.

In our series only in one case could we record an occurrence like this, on an eye in which a polyethylene wick was used.

A hypothetic advantage of a plastic wick is the possibility of achieving drainage and maintaining it securely without iridectomy or iridencleisis. The presence of four larger filtering blebs in Teflon-treated eyes, despite the absence of previously impaired outflow in either of those eyes, seems to testify to good filtration. It should be stressed that the four blebs were large and unmistakable in appearance. In the rest of the cases a shallow bleb may have been present, especially because of the relatively broad base of the plastic material, distributing the filtering aqueous widely over a large surface of tissue. Teflon forms wrinkles (fig. 3) and folds that aid in maintaining drainage.

Statistics

In view of the number of cases and results, it was thought advisable to evaluate the cases in tables statistically by dichotomy. Thus a semiquantitative assessment is possible, which seems more significant than adding the results. The groups can be arbitrarily dichotomized by putting into the first group reactions labelled with a 0 up to 1+, and in the second group from 2+ to the maximum severity of reaction. Concluding from this, we feel that there is no significant difference between the reaction elicited by Teflon and polyethylene.

Summary

Comparison of postoperative reactions four months after intraocular surgery with Teflon and polyethylene gave comparable results. There was little postoperative reaction and no consistent pattern of reaction that could be attributed to the plastics only. A number of complications were listed and the incidence compared. Chloromycetin succinate seemed well tolerated without any toxic or allergic reactions when injected subconjunctivally. Polyethylene, appearing more rigid, was harder to handle in the experimental procedure than the pliable Teflon, which seemed well suited for such an experimental procedure.

1538 Sherbrooke Street, West.

Acknowledgments

We are indebted to Dr. M. J. Lynch and his Department of Pathology for processing the specimens, the sections and the photographic recordings thereof.

References

1. Bietti, G. B.: The present state of the use of plastics in eye surgery. Acta Ophth., **33**:337, 1955.
2. Stone, W.: Alloplasty in surgery of the eye. New England J. Med., **258**:486-490; 533-540; 596-602, 1958.
3. Weizenblatt, S.: Nonspecific granuloma of lacrimal sac harboring polyethelene tube. AMA Arch. Ophth., **58**:130, 1957.
4. Bering, E. A.: The production of tumors in hamsters by implantation of polyethelene film. Cancer, **10**:414, 1957.
5. Lieb, W. A., and Geeraets, W. J.: Die Verwendung plastischen Materials in der Augenchirurgie. Klin. Monatsbl. f. Augenh., **133**:305-340, 1958.
6. Harrison, J., et al.: A comparison of the tissue reactions to plastic materials. AMA Arch. Surg., **74**:139, 1957.

ON THE ENZYMOLOGY OF THE REFRACTORY MEDIA OF THE EYE*

VI. Effect of intralenticular injection of halogen acetates on the transparency and peptidase activity of the rabbit lens

E. Albert Zeller, M.D., and David Shoch, M.D.
(With the technical assistance of Eleanor Andújar)
Chicago, Illinois

In order to gain some information about the maintenance of lenticular transparency, enzymes and enzyme inhibitors were injected in vivo into the rabbit lens. In the course of these studies it was found that the injection of iodoacetate produced opacities within a few days.[2-4] Furthermore, a new peptidase, discovered in the lenses of various species[1, 5-7] was observed to be markedly reduced in these cataractous lenses.[2-4] This enzyme catalyzes the hydrolysis of L-phenylalanine ethylester (PAEE) and other substrates and will be called here for simplicity's sake PAEE-enzyme. In exploring the relationship between the loss in transparency and changes in enzymic activity we included other halogen acetates in our investigations.

Experimental

1. Intralenticular injections

Apparatus. The apparatus used for intralenticular injection of small quantities of fluid is that of Vogel and Reinoehl.[8]

An ordinary micrometer was adapted so that it held a one ml. tuberculin syringe of the Yale Luer-Lock type (Becton, Dickinson and Co., Rutherford, New Jersey). A 20-cm. length of polyethylene tubing (PE 160, Clay-Adams) was attached to the tuberculin syringe by means of an adapter (size B, Clay-Adams Inc., New York 10). This adapter incorporates a one-way ball valve to prevent backflow. The distal end of the tubing was fitted with a similar adapter, to which in turn a 30-gauge needle was attached. It was found that the micrometer limited the movement of the plunger of the syringe so that only about 0.4 ml. of solution could be used. This was more than ample for preliminary washing of the tubing and needle and injection. The micrometer was calibrated and with our apparatus one turn of the measuring screw delivered 0.01 ml. of solution.

Technique. Adult male albino rabbits were used for almost all experiments. About an hour before the experiments began, atropine and phenylephrine were instilled into the conjunctival sacs to provide maximum pupillary dilation. The rabbits were wrapped in a tight-fitting jacket which allowed only the head to protrude. One-percent tetracaine was instilled

* From the Departments of Biochemistry and Ophthalmology, Northwestern University Medical School. This study was supported by a research grant (B-1348) from the National Institutes of Health, the United States Public Health Service. (Fifth paper of this series. See Reference 1.)

into the conjunctival sac of both eyes and about 0.25 ml. of one-percent procaine injected retrobulbarly.

The rabbits were then placed on their sides and a small muscle hook used to proptose the eye. In every case, the right eye was the experimental eye and the left eye the control eye.

A two-mm. radial incision was made with a fine Graefe knife over the ciliary body. This incision was carried almost through the sclera and the tip of the 30-gauge needle placed in the incision. With a slight rotary motion, it was easy to perforate the remaining scleral lamellae and enter the posterior chamber. The needle tip was brought centrally under direct observation until it could be seen lying in the peripheral cortex of the lens usually just at the equator.

At this point the assistant began to rotate the micrometer screw and usually 0.04 ml. of solution was injected. The needle was then rapidly withdrawn and a similar procedure carried out on the opposite eye using a control solution of physiologic saline or buffer.

2. Enzymic measurements

Chemicals. L-Phenylalanine ethylester hydrochloride (PAEE) was prepared in this laboratory. Iodoacetic acid ("highest purity") and bromoacetic acid ("practical") were Eastman Organic Chemicals, chloroacetic acid was a Merck reagent, and sodium fluoroacetate ("technical") was obtained from Tull Chemical Co., Oxford, Alabama. All solutions were made with deionized distilled water and adjusted to pH 6.5.

Preparation of lens homogenates. The rabbits were killed by intravenous injection of air and the eyes were enucleated without delay and frozen at 15°C. The frozen state facilitates the removal of the lens. The latter were homogenized with a Teflon pestle in a glass container with 19 parts (weight/volume) of 0.9 percent sodium chloride solution which is gradually added to the homogenate.

Manometric measurements. The principle of the quantitative determination of the PAEE-enzyme is as follows: by the catalytic action of this enzyme the PAEE is hydrolyzed and the liberated carboxylic group of phenylalanine sets free the equivalent amount of carbon dioxide from the 0.04 M hydrogen carbonate solution in which the reaction takes place. The production of gaseous CO_2 is observed by conventional manometric methods.[1,9] The measurements were carried out at 38°C. and in a CO_2-atmosphere at pH 6.5, the gaseous phase consisting of CO_2. The previously reported set-up[1] was slightly changed.

Main compartment:	0.4 ml. 0.21 M hydrogen carbonate
	0.6 ml. aqua distillata
	1.0 lens homogenate
Side arm:	0.2 ml. 0.21 M hydrogen carbonate
	0.8 ml. 0.0375 M PAEE (final concentration 0.01 M)

Calculations. The reaction rates are given in form of Q-values and are expressed in terms of micromoles of carbon dioxide liberated per hour and per gm. tissue.

Results

1. Morphologic changes

At the time of the injection there was some variation in the appearance of the injected material. About a third of the time the material collected at the tip along the barrel of the needle and seemed to spread the lens fibers apart. A triangular area was thus formed with the base near the capsule and its apex at the point of deepest penetration of the needle. In the remaining cases the solution spread rapidly and seemed to advance as a sheet across the lens in the posterior subcapsular area, and more rarely in the anterior subcapsular area. In no experiments was an intraocular hemorrhage noted. Occasionally, a little aqueous escaped from the posterior chamber along the shaft of the needle.

In almost all cases a slight flare and occasional cells were visible in the anterior chamber after 24 hours. Rarely a more serious inflammation was present and occasionally a true endophthalmitis was obvious. All such

animals were discarded from our series. The track made by the needle was always plainly visible at this time in both lenses. Opacities or vacuoles were not seen. In almost all cases the slight reaction in the anterior chamber of the control eye had subsided after 48 hours. The experimental eye usually still showed a slight flare. The needle tracks were plainly visible in both lenses and no other opacities were noted.

The anterior chamber reaction had usually subsided completely after 72 hours. In the control eye, the needle track was plainly visible and occasionally a few vacuoles could be seen along the needle tracks or in the subcapsular area at the equator at the site of injection.

In the experimental eyes, opacities began to appear. These were always present along the injection track but extended to either side of it forming a large granular V-shaped opacity. In addition, vacuoles were seen to be extending in a bow anteriorly and posteriorly under the capsule. Subcapsular vacuoles were also visible at the posterior pole. These usually formed a small plaque about one third of the lens diameter in size.

After four days the control eyes continued to show only a peripheral streak at the site of injection while in the experimental eyes the posterior lens opacities continued to increase in size.

In some animals the opacities remained the same after one week, while with others the right lens became more and more opaque until a completely mature cataract was formed. In all cases, the control left lenses remained transparent except for a few vacuoles at the site of injection.

Specific observations. Figure 1 shows the frontal and sagittal views of control (left) lenses that have received saline injections only. Generally, these two types of opacities, lenses A and B, occur and they remain stationary during the course of the experiment.

Figure 2 shows the frontal and sagittal views of the opacities found in the experimental eyes. In 72 hours opacities as seen in

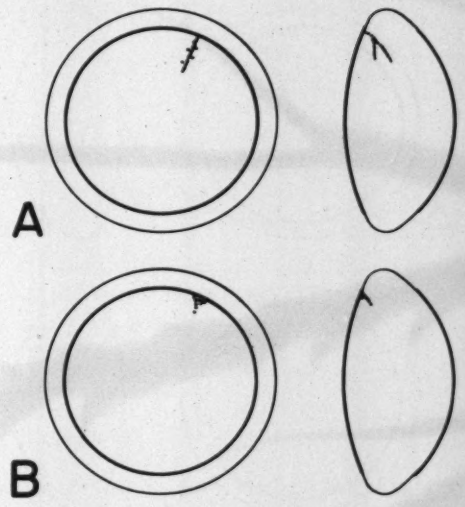


Fig. 1 (Zeller and Shoch). *Control lenses.* Bold lines indicate that part of the lens which is not covered by the dilated pupil. Description of figure is given in the text.

A develop. These are limited to the site of injection with some extension in a linear fashion toward the posterior subcapsular area. In four to five days frequently a ring of vacuoles is seen in the peripheral posterior subcapsular area as shown in lens B. This gradually progresses until by the seventh or eighth day the posterior subcapsular area is completely opaque as seen in lens C.

2. Distribution of the PAEE-enzyme

No difference in the activities of this enzyme for the anterior and posterior part of the rabbit lens was found (Table 1, untreated lens). The statistical analysis with the help of the t-test and F-test confirmed this conclusion. Our data are compatible with the assumption that the lens epithelium contains only a small fraction, if any, of the total PAEE-enzyme activity.

3. Effect of intralenticular injection of iodoacetate on transparency and PAEE-enzyme

When we injected iodoacetate into the lens and removed the eye within three hours and

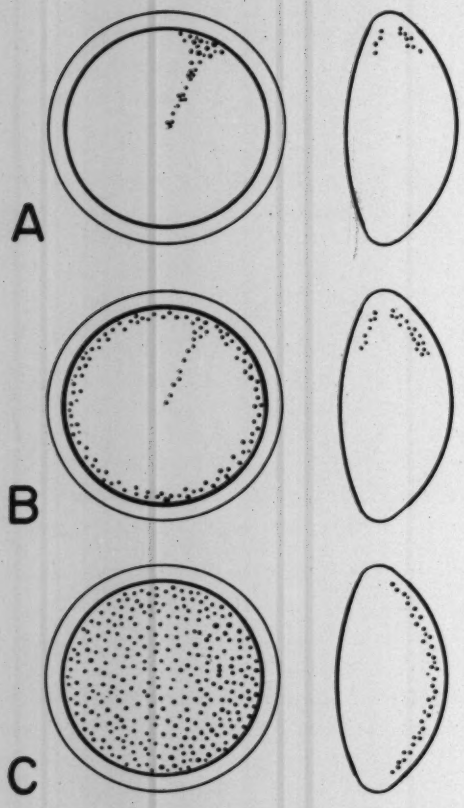


Fig. 2 (Zeller and Shoch). *Opacities in "experimental lens."* See text and legend to Figure 1.

tested the PAEE-enzyme, no significant change in activity was observed. During the following days a gradual drop of the enzyme activity took place and at the fifth day a very low Q-value appeared (fig. 3). The absolute PAEE-activity of the treated eye as well as the relative activity, expressed in percent of the values obtained for the untreated lens, continued to go down slowly until they leveled off after approximately 40 days. No restitution of the PAEE-activity nor of transparency appeared within 67 days. While the opacities are formed mainly in the posterior cortex, the loss of PAEE-enzyme occurs in the frontal anterior as well as in the posterior part (tables 1 and 1A).

Young animals weighing less than 3.0 kg. seemed to respond less both with regard to cataract formation and drop in PAEE-activity. The results gathered with these animals, therefore, were omitted in this report.

4. Effect of other halogen acetates on transparency and PAEE-enzyme

When iodoacetate was substituted by equivalent amounts of bromoacetate, opacities as well as reduction of PAEE-activity were again found (tables 1 and 1a). Both effects are slightly less marked than those noted for iodoacetate. The statistical evaluation revealed a fair significance for the drop of the activity of the PAEE-enzyme for the anterior fraction of the lens (table 1A).

One glance at Table 1 reveals that chloroacetate and the powerful poison, fluoroacetate, exert little influence on the lens. In general the enzymic changes seem to be more marked in the anterior than in the other part of the lens. No significance, however, was computable statistically for the two lens halves except for fluoroacetate which did not cause any difference in PAEE-activity between treated lens and untreated lens, but

TABLE 1

PAEE-activity in lens 17 days after intralenticular injection of halogenoacetates

(The figures represent Q-values ± standard deviations. Values from one to three were assigned to the intensity of cataract formation.)

Halogenoacetates	No. of Determinations	Treated Eye		Untreated Eye		Degree of Cataract
		Anterior	Posterior	Anterior	Posterior	
F	4	379 ± 113	323 ± 134	397 ± 149	343 ± 127	0.5
Cl	6	410 ± 94	434 ± 147	407 ± 200	427 ± 82	1.2
Br	6	212 ± 176	240 ± 190	434 ± 140	415 ± 144	2.3
I	8	235 ± 133	258 ± 166	487 ± 107	451 ± 184	2.5

between the two halves of the treated lens ($P<0.05$).

Discussion

Before we enter the discussion of our results, a general remark about three different kinds of cataract formation should be made.

When the lens epithelium is damaged, for example by radiation[3,10,11] or by systemic application of iodoacetate,[12] it takes several weeks until marked opacities appear. On the other hand, after intralenticular injection of certain enzyme inhibitors, a cataract develops within a few days which, in view of the locus of the injection, is not likely directly connected with the epithelial functions. It seems as if the epithelium as a pacemaker influences the metabolism of the lens body; if the cells discontinue their activity, the lenticular body reverts to its own intrinsic metabolism as indicated by the loss of transparency. It is assumed that the effect of the epithelium on the metabolism of the lens body is mediated by chemical substances. Thus, we have three possible types of cataract genesis:

1. Dysfunction of the epithelium.
2. Metabolic aberrations in the lens body.
3. Disturbance in the transmission of chemical signals from epithelium to lenticular body.

Obviously, the cataract production described here belongs to the second type. Its mechanism is still under investigation. By assuming that the iodoacetate distributes evenly over the lens body approximately a concentration of 0.01 M would be attained. At this concentration the glycolytic system

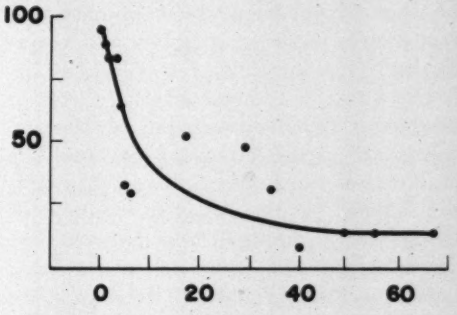


Fig. 3 (Zeller and Shoch). *Course of PAEE-activity after intralenticular injection of iodoacetate.* Ordinate: PAEE-activity of the treated lens expressed as percent of activity of untreated lens, abscissae: days after injection. The Q-values were determined with whole lenses.

of the lens—the main energy providing sequence of the lens body[13]—is most likely blocked by iodoacetate. This conclusion is borne out by the observation that in cultured lenses lactic and pyruvic acids decrease when treated with this agent.[14,15] Iodoacetate exerts in vitro also a slight inhibitory action on the PAEE-enzyme of rabbit lenses (pI_{50}-value = 2.2, unpublished data). However, the in vivo administration of iodoacetate does not cause an immediate drop in PAEE-enzyme (fig. 3).

While the primary point of attack of iodoacetate remains to be found, one enzymic reaction accompanies cataract formation regularly. Every time marked opacities develop, the drop in the rate of PAEE-hydrolysis becomes statistically significant. This is not only true for cataracts caused by intralenticular injections of halogenoacetates (tables 1 and

TABLE 1A

Statistical treatment of data of Table 1

(The calculations were carried out to the third decimal place, but only two positions are given below. The data refer to treated vs. untreated lenses)

Halogeno-acetates	Anterior Part		Posterior Part		Whole Lens	
	t, P	F, P	t, P	F, P	t, P	F, P
F	0.34	0.13	1.93	3.70	0.68	0.46
Cl	0.04	0.002	0.15	0.02	0.13	0.02
Br	3.87, <0.02	14.98, <0.05	2.53, <0.1	6.38, <0.1	3.20, <0.05	10.13, <0.05
I	4.77, <0.01	22.61, <0.01	3.34, <0.04	11.17, <0.05	4.50, <0.01	20.30, <0.01

1A) but also for human senile cataracts and for opacities produced in rabbits with x-irradiation.[1] This biochemical resemblance of different forms of cataract may be related to similarities found between the morphologic features of various groups of cataracts. The characteristics and progression of the opacities initiated by intralenticular injections of iodoacetate are similar to those observed after systemic application of this substance.[12] These latter morphologic changes in turn were considered to resemble those by x-irradiation.[12]

The significance of the changes of PAEE-activity in the chemical process leading to a loss of transparency is not clear, partly because we do not know much about the biologic role of intracellular peptidases.[16] The PAEE-enzyme which at the present time is being thoroughly studied in this laboratory[17] belongs to the group of aminopeptidases but is distinctly different from previously known members of this group.[7,18] Whatever the function of this enzyme turns out to be, it is almost certain that it is involved in protein metabolism.

At the present time there is no information available to settle the question—if it is a meaningful question—of whether the change in peptidase activity is an integral part of the mechanism leading to the loss of transparency or whether it is a consequence of the cataractous state or whether the two events are entirely unrelated to each other. The second possibility seems to be less likely since, in the anterior fraction of the lens, a reduction of PAEE-activity is observed without appearance of opacities. But we do not want to exclude the idea that the drop in enzymic activity is an adaptive process. The marked drop in the concentration of certain proteins in the cataractous lens[19] could lead to adaptive changes in the activity of enzymes which catalyze the degradation of proteins. Only by further analysis of the biochemistry of cataract formation and comparative biochemical studies can we hope to penetrate more deeply into this question. We may learn from changes in peptidase activities which occur immediately after fertilization of the sea urchin egg[20] or during the regeneration of the tail of the Xenopus tadpole.[21] Finally it may be mentioned that, by disturbing the energy transfer with dinitrophenol, the liberation of free amino acids by liver slices, presumably through peptidase activity, is strongly reduced.[22]

If a dynamic protein turnover in the lens occurs, as many observations suggest, the enzymic systems leading to protein synthesis as well as to protein degradation may be considered as parts of a more general machinery which maintains the integrity of the lens proteins. Before they can degenerate into light scattering proteins, they are scrapped and resynthesized. This concept might be applicable to other proteins in other tissues whose structural intactness is essential for their biologic functions.

Not every enzyme blockade or administration of powerful enzyme inhibitors causes a loss of transparency. In reducing the carbonic anhydrase activity of the lens with intralenticular injection of acetazolamide no cataract was produced.[23] Fluoroacetate which disrupts the citric acid cycle most effectively is without apparent influence on the lens in vivo. This cycle seems, therefore, of little importance for the maintenance of the transparency of the lens. This conclusion is in agreement with the assumption that the Krebs cycle does not contribute much to the lenticular energy transformation.[13] In fluoroacetate-containing media cultured lenses become slowly opaque.[15] This cataract belongs probably to type (1) of our system. It stands to reason that, in intact epithelial cells, the citric acid cycle or a related system is operating.

In discussions with one of us (E.A.Z.) Dr. Ludwig von Sallmann pointed out that the changes we noted might simply be the results of trauma and not due to the injection of iodoacetate per se. This remark induces us to discuss the specificity of the cataractous process described here. Undoubtedly, after every intralenticular injection opacities de-

velop. However, in the control left eyes, these opacities are limited to the site of injection and appear as small vacuoles along the needle track. These opacities remain fixed in position and do not spread into the lens no matter how long the rabbits are observed up to periods of three to four months. On the other hand the opacities produced by the injection of iodoacetate appear not only at the injection site but also at the posterior subcapsular region and continue to develop so that in less than a week a true gross clinical cataract is evident which in many cases goes on to form a dense, mature cataract.

The specificity of iodoacetate in producing these changes is further supported by the failure of acetazolamide,[23] chloroacetate and fluoroacetate to produce the same picture. The opacities found by injection of the latter two substances are similar to those produced by saline.

For these reasons we feel that trauma alone cannot be implicated as the cause of the gross cataracts which follow the intralenticular injection of iodoacetate and bromoacetate. At the present time work is going forth to demonstrate the histologic changes which take place and it is hoped that this will further differentiate the iodoacetate cataract from the control opacities and vacuoles formed by the trauma of injection.

Summary

1. The intralenticular injection of iodoacetate into the rabbit lens in vivo produces a characteristic opacification which develops in three to four days. This opacity usually goes on to complete cataract formation in a short time. Such cataracts are not found after the injection of physiologic saline or buffer solutions used as controls.

2. Frontal and posterior parts of the rabbit lens display the same catalytic activities toward L-phenylalanine ethylester (PAEE). This observation excludes the possibility that this enzyme is located mainly in the epithelium.

3. After the intralenticular injection of 2.5 micromoles of iodoacetic acid into the rabbit lens marked reductions of the PAEE-activity in both halves of the lens appear approximately at the same time as the opacities. The enzymic activity continues to drop until about 40 days after the injection. No reversion of cataract or loss of PAEE-activity has been observed.

4. Intralenticular injections of bromoacetate lead both to loss of transparency and to PAEE-activity reduction. Both changes are less marked than those obtained with iodoacetate.

5. The other halogenoacetates, chloro- and fluoroacetates, exert little influence on transparency and on PAEE-activity.

6. Some possible relationships between cataract formation and depression of the PAEE-enzyme are discussed.

303 East Chicago Avenue (11).

Acknowledgment

We wish to acknowledge with gratitude the help of two senior medical students, Leonard Naiman and Bruce Parker. Their services were made available to us by the support of The National Council to Combat Blindness under its Fight for Sight Student Fellowship program. The specific grant numbers were SF-184 and SF-185. We should like to express our appreciation to the Council for their foresightedness and generosity in promoting an interest in ophthalmologic research among medical students.

References

1. Zeller, E. A., and Devi, A.: On the enzymology of the refractory media of the eye, V. On the occurrence of proteolytic enzymes in normal and cataractous lenses. Am. J. Ophth., **44**:281-283 (Nov. Pt. II) 1957.

2. Zeller, E. A., and Shoch, D.: On the occurrence and biological function of lenticular peptidases. Acta XVIII Consilium ophth., **I**:713-717, 1959.

3. ———: On the role of cathepsins in protein metabolism. Fed. Proc., **18**:358, 1959.

4. Shoch, D., and Zeller, E. A.: On the production of cataracts by the intralenticular injection of certain enzymes and enzyme inhibitors. Am. J. Ophth., **47**:876, 1959.

5. Zeller, E. A.: Enzymology of the refractory media. Am. J. Ophth., **43**:785-786, 1957.

6. Devi, A.: Characterization of the intracellular proteolytic enzyme in the lens. Am. J. Ophth., **48**: 29-32 (Nov. Pt. II) 1959.
7. Zeller, E. A., Banerjee, R., and Shoch, D.: Enzymology and comparative biochemistry of a new lens peptidase. Biochem. J., **76**: 49P, 1960.
8. Vogel, A. W., and Reinoehl, D. A.: In vivo intralenticular studies. Am. J. Ophth., **44**:298-306 (Nov. Pt. II) 1957.
9. Parks, R. E., Jr., and Plaut, G. W. E.: A manometric assay for chymotrypsin. J. Biol. Chem., **203**: 755-761, 1953.
10. von Sallmann, L., Tobias, C. A., Anger, H. O., V[illegible], C., Kimura, S. F., Munoz, C. M., and Drungis, A.: Effects of high-energy particles, X-rays and a[illegible]g on lens. Arch. Ophth., **54**:489-514, 1955.
11. Puntenney, I., and Shoch, D.: The ciliary body in radiation cataract. Am. J. Ophth., **38**:673-682, 1954.
12. Cibis, P. A., Constant, M., Pribyl, A., and Becker, B.: Ocular lesions produced by iodoacetate. Arch. Ophth., **57**:508-519, 1957.
13. Kinoshita, J. H., and Wachtl, C.: A study of the C^{14}-glucose metabolism of the rabbit lens. J. Biol. Chem., **233**:5-7, 1958.
14. Nakamura, M.: Metabolism of crystalline lens, effect of inhibitors on respiration and glycolysis. Acta Soc. Ophth. Japan, **59**:1658-1666, 1955. Abstract in Am. J. Ophth., **41**:565-566, 1956.
15. Nordmann, J., Mandel, P., and Achard, M.: Inhibition of sugar metabolism in the lens. Brit. J. Ophth., **38**:673-679, 1954.
16. Fruton, J. S., and Simmonds, S.: General Biochemistry. New York, Wiley, 1958, p. 702.
17. Zeller, E. A., and Banerjee, R.: Enzymology of the refractory media of the eye: VII. Metal activation of hydrolysis of L-phenylalanine ethylester by beef lens. In press.
18. Zeller, E. A., and Banerjee, R.: Substrate and activator specificity of a new cathepsin. Abstracts, 137th Meeting, Am. Chem. Soc., Cleveland, 1960: 43 C.
19. Pirie, A., and van Heyningen, R.: Biochemistry of the Eye, Springfield, Ill., Thomas, 1956, p. 18.
20. Maggio, R.: Mitochondrial and cytoplasmic protease activity in sea-urchin eggs. J. Cellular Comp. Physiol., **50**:135-143, 1957.
21. von Hahn, H. P.: Der Einfluss morphostatischer Stoffe auf Proteasen regenierender Gewebe. Oncologia, **12**:120-128, 1959.
22. Steinberg, D., Vaughan, M., and Anfinsen, C. B.: Kinetic aspects of assembly and degradation of proteins. Science, **124**:389-395, 1956.
23. Mamo, J. G., and Leopold, I. H.: Carbonic anhydrase activity in the lens. Acta XVIII Consilium ophth., **I**:718-725, 1959.

THE TECHNIQUE OF FLUORESCENT ANTIBODIES IN OPHTHALMOLOGY*

A STUDY OF HERPES SIMPLEX AND VACCINE KERATOCONJUNCTIVITIS AND HUMAN TRACHOMATOUS INFECTION

RICCARDO VOZZA, M.D., AND DIEGO BALDUCCI, M.D.
Rome, Italy

The technique of fluorescent antibodies, with the aid of a fluorescent microscope, offers the possibility of localizing viral antigenic material in infected cells. This possibility has been realized by the Weller and Coons[5] indirect technique putting the viral antigen contained in the cells of trypsinized tissue cultures into contact with the specific antiserum. Another antiserum substituting fluorescein-labelled antibodies for the ones previously used is then flooded over the same cells. Fluorescein-labeled gamma globulins will then precipitate in the sites where the previous antigen-antibody reaction took place. The unbound components of both sera are then removed by flooding the specimen with a phosphate isotonic buffer. Examination under fluorescent light allows easy identification and localization of fluorescein in the infected cells.

Viral diseases of the keratoconjunctival area are most suitable for application of this technique because of the ease in obtaining smears of infected cells. This research was

* From the Department of Ophthalmology, University of Rome, Head: Prof. G. B. Bietti, and the Department of Microbiology, Istituto Superiore di Sanita, Head: Prof. G. Penso.

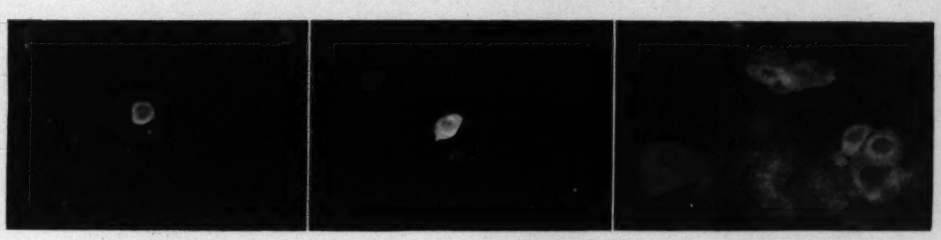


Fig. 1 (Vozza and Balducci). Cells with cytoplasmic fluorescence observed in smears from vaccine keratoconjunctivitis.

undertaken to verify the efficiency of the fluorescent antibody technique in detecting small amounts of antigenic material.

Materials and Methods

Viruses

Vaccine keratoconjunctivitis was induced by direct corneal scratch in adult guinea pigs with a dermatotropic virus (I.S.S. strain). Herpes simplex keratoconjunctivitis was also induced by direct corneal scratch in a group of adult rabbits with the lyophilized "Z" strain of virus passed once on the chorioallantoic membranes of chick embryos. Another group of rabbits was infected, also by direct corneal scratch, by means of a lancet dipped in the fluid of the vesicles of a subject affected with recurrent herpes labialis.

Cells

The infected cells were obtained by smearing the scrapings from inoculated animals onto coverslips. Conjunctival smears from trachomatous patients (I and II) were collected in North Africa (Lybia). The smears in all cases were dried at 37°C. for one hour and were fixed in acetone for 10 minutes, at room temperature. They were then dessicated again at 37°C. for one hour and stored at 4°C., if staining was not carried out immediately. Storage at 4°C., however, never exceeded more than 14 days.

Antisera

Antisera for vaccine were prepared from rabbits with repeated cutaneous inoculations and intravenous injections of the virus. The sera were collected after two months. Before usage they were diluted 1:5 in isotonic phosphate buffer.

Human sera positive for herpes simplex were employed with a titer of complement fixing antibodies ranging from 1:20 to 1:32. For the usage they were diluted from 1:3 to 1:5 according to the titer, in isotonic phosphate buffer.

The trachomatous antiserum was prepared from four rabbits and four monkeys (Rhesus). Conjunctival cells, obtained by scrapings from the conjunctiva of 100 trachomatous subjects (I and II) were suspended in 10 ml. of Hanks solution containing 200 σ/ml. of streptomycin. The suspension was submitted to three rapid freezings and thawings in order to release the intracellular virus particles. The suspended material was then centrifuged at 3,000 rpm for 10 minutes and the supernatant homogenized with coadjuvants in oil following Freund's technique. Two intramuscular injections were done at weekly intervals. The sera were then collected after two months. For use they were diluted 1:5 in isotonic phosphate buffer.†

†This procedure was adopted in 1958 when no viral strains were available to us. At the present time, experiments are under way to check the reported data with an antiserum obtained from animals inoculated with a purified suspension of elementary bodies. For this purpose, the viral strain Trachoma Asmara 3/1960, isolated by one of us (R.V.) in Ethiopia, has been used. Isolation and purification procedure is reported in the paper: Felici, A., and Vozza, R.: Virological studies on trachoma (1961) Issued by Haile Selassie 1st Ophthalmic Center Asmara, Ethiopia. In press.

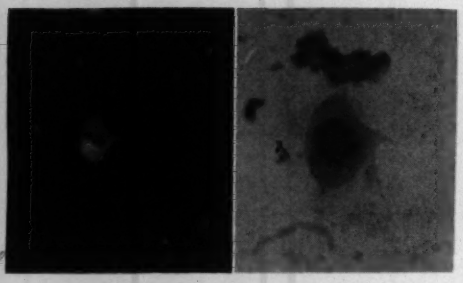


Fig. 2 (Vozza and Balducci). (Left) Cells with cytoplasmic fluorescence counterstained with Giemsa. (Right) showing evidence of inclusion bodies.

Fluorescein-labeled gamma globulins

For staining the vaccine-infected cells, sheep antirabbit fluorescent serum was employed. Before usage, the serum was adsorbed twice on acetone-precipitated guinea-pig liver powder in order to remove unspecific staining.

For the study of herpes-simplex keratoconjunctivitis, horse-antihuman fluorescein-labeled serum was used. In order to remove aspecific staining, it was adsorbed twice on acetone-precipitated rabbit's liver powder. For the trachomatous scrapings, when a rabbit antiserum was used, the detector serum was a fluorescein-labeled sheep-antirabbit serum.

Adsorption was tried, before employment, on acetone-extracted powders of human, mouse, ferret, rabbit and monkey's liver. When sera of trachomatous individuals were used as a possible source of antibodies, staining was done with horse-antihuman fluorescein-labeled serum. Adsorption was tried on mouse and ferret liver acetone-extracted powder. All the fluorescent sera were diluted 1:5 in pH 7.1 isotonic phosphate buffer. The adsorption was carried out at 37°C. for 30-60 minutes. The suspension was kept in motion in a shaker contained in the thermostat. All the fluorescent sera were obtained from the Sylvana Chemical Company, Orange, New Jersey (U.S.A.).

Staining with fluorescent antibody

The smears, after fixation and drying, were first flooded with the antisera for 30 minutes at room temperature in Petri dishes containing moist cotton in order to avoid evaporation. The unbound globulins were washed out for 10 minutes with three changes of isotonic phosphate buffer. The smears were then allowed to contact for 30 minutes with fluorescein-labeled gamma globulins at room temperature. After another washing with isotonic phosphate buffer (10 minutes, three changes), the coverslips were mounted in pH 7.1 buffered glycerol.

Controls

Controls were always prepared with uninfected cells which were stained simultaneously and with the same technique as the uninfected material.

Controls of the infected materials were also prepared, substituting for the antiserum another void of specific antibodies. All the

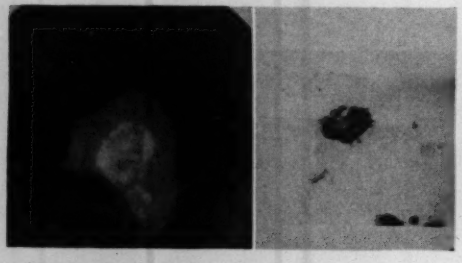


Fig. 3 (Vozza and Balducci). (Left) Cell showing mostly nuclear fluorescence. (Right) Counterstained with Giemsa. There are nuclear aspecific alterations.

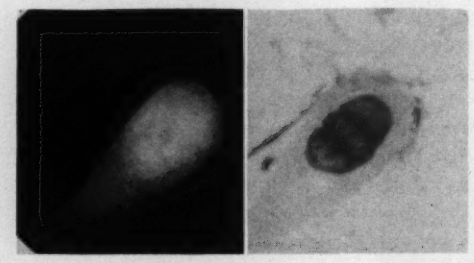


Fig. 4 (Vozza and Balducci). (Left) Giant herpetic cell stained intensely with fluorescent antibody. (Right) The same cell counterstained with Giemsa shows lack of morphologic alterations.

controls were constantly negative for herpes simplex and vaccine keratoconjunctivitis. The nonspecific staining was easily recognizable from the specific green one because of the typical yellow-brown hue.

The results were inconstant in trachoma, as well as in the controls with uninfected conjunctival cells, because the presence of aspecific staining was occasionally observed. This phenomenon will be discussed later.

Optical equipment

The Zeiss optical equipment for fluorescence was employed. The light source was an OSRAM HBO 200. The excitation filters were the Schott BG 12: the stopping filters were the Schott OG4 and OG5. Photographs were taken with a 6.0 by 6.0 camera on Agfa panchromatic 17/10 DIN films.

Results

Vaccine keratoconjunctivitis

A considerable number of cells staining with a specific green fluorescence were observed on the smears obtained from cases of severe vaccine keratoconjunctivitis. The fluorescence was almost exclusively cytoplasmic, mainly with a granular nature. In some cells, fluorescence was concentrated in bright blocks in areas close to the nuclear membrane. Counter-staining of these cells with Giemsa demonstrated inconstantly the presence of Guarnieri bodies.

Generally, the fluorescent material filled the cytoplasm with very brilliant micro-granulations; in the advanced stages of infection the nucleus was also involved. Counterstaining with Giemsa in these cases showed shrinking of the cytoplasm with nuclear pyknosis and lysis. Some cells, without evident morphologic alteration, exhibited an homogeneous fluorescence of the cytoplasm. Specific green fluorescence was, often, observed in the cytoplasm of round cells of inflammatory origin.

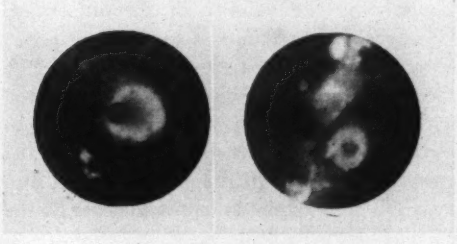


Fig. 5 (Vozza and Balducci). Cells staining with fluorescent antibody in conjunctival smears obtained from trachoma patients.

Herpes simplex keratoconjunctivitis

Specific staining was seldom observed 12 hours after the corneal inoculation. Progressive increase, both quantitative and qualitative, was recorded on specimens obtained from 24 to 72 hours after the inoculation. The fluorescence appeared to decrease in the following days and, after seven days, was completely absent with both strains of viruses.

Fluorescence, particularly in the early stages of the infection was localized almost exclusively in the nuclei as small brilliant granulations. Counterstaining with Giemsa and observation under bright illumination revealed only occasional typical inclusion bodies. More frequently, particularly in the advanced stages, there were such nuclear alterations as pyknosis and kariolysis.

The presence of antigenic material in the cytoplasm in advanced cases was frequently observed. Cytoplasm particulate fluorescence was also observed in the cytoplasm of round cells of inflammatory origin. Giant cells were seldom recognized in a dark field but always exhibited a marked fluorescence, both nuclear and cytoplasmic. Even in these cases there was a lack of typical inclusion bodies in the slides counterstained with Giemsa.

As with vaccine keratoconjunctivitis, cells of conjunctival origin were found to stain both with particulate and homogeneous fluorescence.

Trachoma

In the smears obtained from trachomatous subjects, the picture was not as clear as in

the previous experiments employing rabbit antiserum. The controls with uninfected cells were not constantly negative, showing in some experiments evidence of a somewhat green fluorescence. An attempt to interpret this phenomenon will be made later.

In some experiments with negative controls, however, infected cells were found with a slightly particulate fluorescence limited to the cytoplasm. These cells, isolated with the diamond marker and counterstained with Giemsa, failed to show evidence of inclusion bodies.

It was practically impossible to localize in a dark field, as under fluorescent light, cells with inclusion bodies. Thus, we were not able to control the behavior of these elements under our experimental conditions, despite the large number of smears stained with fluorescent antibodies. Owing to the small incidence of these cells in the smears, the possibility of their detection, under the present experimental conditions, has to be considered exceptional. The results were no more satisfactory with the sera of trachomatous subjects and horse-antihuman fluorescein-labeled serum.

Discussion

The fluorescent antibody technique was demonstrated to be a valuable means to identify on smears the intracellular viral material of both herpes simplex and vaccine experimental keratoconjunctivitis.

The results were not dissimilar to the in vitro findings of Noyes and Coll[2] for vaccine and Lebrun[1] and O'Dea and Coll[3] for herpes simplex.

In herpes simplex keratoconjunctivitis, in the slides counterstained with Giemsa, inclusions were seldom seen in cells with particulate nuclear fluorescence. This is according to Thygeson's[4] reports on smears from cases of herpes simplex keratitis, both experimental and human. The lack of typical nuclear inclusions in the smears seems to be due to the fact that the marginated chromatin of the nuclear envelope masks the inclusion bodies, which are otherwise well evident on nuclear histologic cross sections.

In our cases many cells with particulate nuclear fluorescence showed, when counterstained with Giemsa, faintly stained inclusion bodies. However, in other elements there was a complete lack of morphologic indication of the presence of nuclear and cytoplasmic fluorescence. Sometimes these cells exhibited only such aspecific degenerative changes as shrinking of the cytoplasm and nuclear kariolysis and pyknosis. These findings suggest the possibility that the formation of inclusion bodies is only one of the morphologic changes induced by the viral infection.

There is theoretical interest in the finding that giant cells stained intensely, even in the absence of morphologic changes. This could confirm once again the role of the virus at the onset of the cellular atypical proliferation.

Probably because of their cytoplasmic situation, inclusion bodies were clearly seen in the smears of vaccine keratoconjunctivitis. Their fluorescent staining again demonstrates their viral origin. Also, in the case of vaccine, the presence of cells undergoing degenerative changes without corresponding formation of inclusion bodies suggests the same deductions as for herpes simplex. The presence in both types of keratoconjunctivitis of cells showing an homogeneous staining seems to be in relation to the reaction of the sera with the soluble antigens.

The weak point of the present research on trachomatous smears was the uncertainty surrounding the validity of the antiserum. However, its control was impossible in absence of a reference antigen. The presence of specific staining in some controls prepared with uninfected cells was probably related to conjunctival-cell antibodies developed by the animals injected with the trachomatous material, in spite of the attempts to separate the cellular debris by centrifugation.

Unfortunately, adsorption on many kinds of tissue powders, both of the rabbit serum

and of the fluorescent gamma globulins, was not effective in the control of undesired staining.

Human sera of trachomatous individuals failed to produce significant antigen-antibody reaction at cellular levels, probably because of their low titer. Attempts with this system were therefore soon abandoned because of the uncertain results and the possibility of direct reaction between the horse-antihuman gamma globulins and the conjunctival cells.

Although a very small amount of antigenic material is probably contained in the cells we hope that, at least in severe acute cases, an antiserum obtained from pure virus devoid of proteins of human origin may give dependable results following the same technique.

The presence of specific staining in some trachomatous smears when all controls were negative, seems not without interest, particularly because these cells did not demonstrate evidence of inclusion bodies. The presence of a soluble phase of the trachomatous virus could be supposed if our findings can be confirmed.

Summary

The fluorescent-antibody technique was used to study experimental herpes simplex, vaccine keratoconjunctivitis and human trachomatous infection. The technique proved to be effective in identifying cells experimentally infected by the virus. Inclusions stained intensely, demonstrating the presence of antigen at their level, as did giant herpetic cells. The results on trachomatous smears were uncertain. The presence of a soluble phase of the trachoma virus seems probable.

Eye Clinic,
University of Rome.

Acknowledgment

We wish to express our gratitude to Prof. S. Chiavarelli for his valuable assistance and advice.

References

1. Lebrun, J.: Cellular localization of herpes simplex virus by means of fluorescent antibodies. Virology, **2**:496, 1956.
2. Noyes, W. F., and Watson, B. K.: Studies of the increase of vaccine virus in unfixed preparations of trypsinized tissue cultures. J. Exper. Med., **102**:237, 1955.
3. O'Dea, J. F., and Dineen, J. K.: Fluorescent antibodies studies with herpes simplex virus in unfixed preparations of trypsinized tissue cultures. J. Gen. Microbiol., **17**:19, 1957.
4. Thygeson, P.: Cytologic observations on herpetic keratitis. Am. J. Ophth., **45**:240, 1958.
5. Weller, T. H., and Coons, A. H.: Fluorescent antibodies studies with agents of varicella and herpes zoster propagated in vitro. Proc. Soc. Exper. Biol. & Med., **98**:219, 1954.

STUDIES UPON METHYL- AND FLUORO-SUBSTITUTED PREDNISOLONES IN THE AQUEOUS HUMOR OF THE RABBIT*

II. Chromatography

Henry S. Kroman, M.S., and Irving H. Leopold, M.D.
Philadelphia, Pennsylvania

Introduction

The present investigation was undertaken to determine the spectrophotometric and chromatographic properties of the methyl- and fluoro-substituted prednisolones and their concentration in rabbit primary aqueous humor.

In previous work carried out in this laboratory the penetration into the aqueous humor and the level in the blood as determined by a blue tetrazolium colorimetric technique were reported. Chromatography and spectro-

* From the Research Department, Wills Eye Hospital. This investigation was supported in part by Research Grant B-2058 from the National Institute of Health, United States Public Health Service.

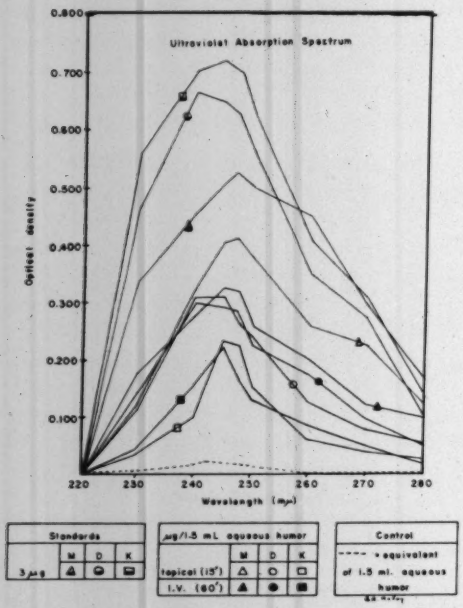


Fig. 1 (Kroman and Leopold).

photometry were used in this investigation to determine the concentration of steroids in the aqueous humor.

The methods employed in this investigation are considered to be more sensitive than the colorimetric technique as used in the previous investigation. Previous work, involving these two methods, also displayed the superiority of a chromatographic and spectrophotometric method over the blue tetrazolium technique.

Materials

Solvents. Toluene and propylene glycol were purchased from Eastman Kodak Laboratories. Absolute methanol and chloroform, Mallinckrodt Chemical Works, were redistilled before use. Whatman No. 1 filter paper was fashioned into four parallel arms, 1.0- by 30 cm. each, attached to a common head as described by Burton and coworkers. Blue tetrazolium, Nutritional Biochemicals Corporation, was prepared as a 0.2-percent aqueous solution and mixed with two volumes of 10-percent sodium hydroxide before use.

Chromatographic equipment. A chromatocab, Arthur H. Thomas, was equipped with glass solvent troughs and glass antisiphon rods.

Spectrophotometry. A mineralight, Ultraviolet Products Corporation, South Pasadena, California, was used to examine the completed chromatogram under ultraviolet light. A Beckman spectrophotometer, Model DU, was used to measure the absorption and optical densities of solutions contained in quartz microcurettes with one-cm. light paths and a total volume of one ml.

Experimental

Pigmented rabbits each weighing four to six lb. were used. For each experiment new animals were employed, with each animal being used only once. Prior to tapping the anterior chamber, each eye was anesthetized with one drop of a 0.5-percent solution of pontocaine hydrochloride and then thoroughly washed with isotonic saline. Removal of the aqueous humor was accomplished by means of a 26-gauge needle attached to a tuberculin syringe.

Intravenous injection. To each normal animal was administered, intravenously, 25 mg. of steroid suspended in isotonic saline. After the elapse of 60 min. the anterior chamber was tapped and the primary aqueous humor removed, pooled and analyzed. A total of 1.5 ml. of primary aqueous humor was used for each analysis.

Topical application. Each steroid, suspended in isotonic saline, in a concentration of 0.5 percent was instilled into the cul-de-sac every 15 minutes for one hour. Fifteen minutes after the last application the aqueous humor was withdrawn, pooled and analyzed. A total of 1.5 ml. of primary aqueous humor was used for each analysis.

The samples collected were extracted three times with five volumes of redistilled chloroform. The extract was concentrated to a volume of approximately 0.5 ml. under reduced pressure and at a bath temperature of 45°C. The concentrated extract was then ap-

plied to the chromatogram at a point 30 cm. from the bottom. A stream of warm air from a domestic hair dryer was used to dry the spot after application and to help to reduce the horizontal expansion of the material on the paper. The filter paper, prior to use, was washed for 24 hr. with 95-percent ethanol and air dried. Impregnation with propylene glycol was accomplished by immersion in the solvent and removal of the excess solvent by pressing between two sheets of dry filter, as described by Pechet.

The detection and quantitative estimation of the materials present were accomplished by the following methods: (1) examination under ultraviolet light, (2) spraying with a blue tetrazolium-sodium hydroxide reagent, (3) elution of the spot located by (1) and (2) above, on a parallel chromatogram, with one ml. of absolute methanol for 20 min. and determining the absorption spectrum between 220-280 mμ.

Results

Chromatography. The paper chromatography of samples of aqueous humor taken from animals treated with Decadron, 16 α methyl 9 α fluoro prednisolone, Kenacort, 9 α fluoro 16 α hydroxy prednisolone, and Medrol (free alcohol) 6-methyl prednisolone, administered topically and systematically, revealed a spot, after reaction with blue tetrazolium-sodium hydroxide and examination under ultraviolet light, that had the general mobility characteristics of the respective standards in chromatograms covering a period of 12 to 48 hr. The intensity of the zones indicated the concentration of each steroid to be approximately one gamma when chromatographed separately and in combination with standard material.

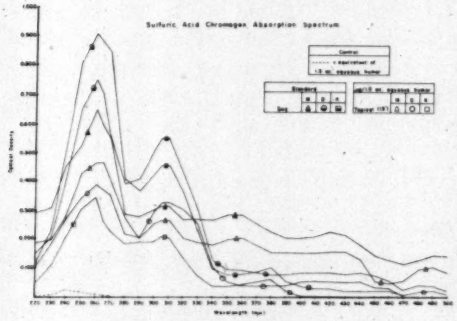


Fig. 2 (Kroman and Leopold).

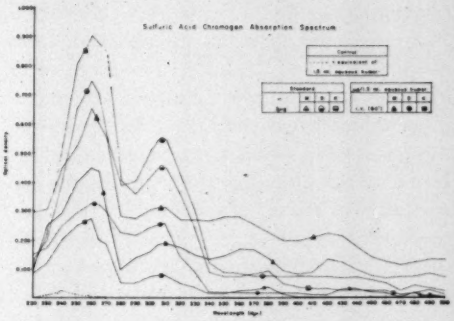


Fig. 3 (Kroman and Leopold).

Ultraviolet absorption spectrum. The zones after chromatography, located by ultraviolet scanning, were eluted with absolute methanol and measured spectrophotometrically between 220 and 280 mμ. Results are presented in the form of an absorption curve in Figure 1. These results clearly indicate the presence of an absorption maximum between 220 and 240 mμ which would correspond to the Δ^4-3 keto grouping. Since Medrol (free alcohol), Kenacort and Decadron can all be shown to obey Beer's law, at last for concentrations up to 10 μg., it is apparent from the height of the curves following systemic injection, that approximately* 1.0 μg. of all steroids penetrated into the aqueous humor. Following topical application, the Kenacort and Decadron apparently also reached a concentration of approximately 2.0 μg. In previous experiments it was found that recovery of the steroid after elution was approximately 80-percent.

Sulfuric acid chromagen absorption spectrum. The absorption curves of the chromagen produced by the reaction of the eluted zones with concentrated sulfuric acid are presented in Figures 2 and 3. It is obvious that all three curves for the standard possess the

* Represents the aqueous humor from eight rabbit eyes.

same maxima; 260, 305, 360, 420 and 490 mμ. Following the systemic injection of Decadron, Medrol and Kenacort, the concentration of these steroids in the aqueous humor was observed to be between 1.0 and 1.5 μg. with all three steroids. When Decadron, Medrol and Kenacort are administered topically, the concentration of steroid penetrating into the aqueous humor appeared to be greater than when the steroid had been administered systemically although the difference is not significant.

Discussion

Paper partition chromatography has been widely used as a means of identifying various materials. The methods developed by Zaffaroni and coworkers and as modified by Green and coworkers employing both chromatography and spectrophotometry, are sufficient to identify steroid material with confidence as well as proving the homogeneity of a sample.

The paper chromatography of eluates of pooled aqueous humor from animals treated systemically and topically with Medrol, Decadron and Kenacort revealed a concentration in the aqueous humor of approximately 1.0 μg/1.5 ml. of pooled aqueous humor. This value was substantiated by the ultraviolet absorption and sulfuric acid chromagen absorption curves. In a previous investigation, employing a blue tetrazolium colorimetric technique, very much higher concentrations of both Decadron and Medrol were observed in the animal. High values, such as these, were observed by Green and coworkers in experiments conducted in this laboratory when using the blue tetrazolium technique for analysis but subsequently more sensitive techniques revealed a very much lower concentration of steroid material. In this previous work glucose was found to be an interfering substance when measuring steroids by the blue tetrazolium technique. The high values observed while investigating the methyl and fluoro prednisolones and employing this colorimetric technique cannot be attributed to the interference of glucose and as yet cannot be explained. Further investigation will be required to determine the explanation for the high values observed employing the colorimetric technique.

The absorption curve observed after reacting the eluate of the steroid spot with concentrated sulfuric acid is most interesting in that a maximum is observed at 260 mμ, whereas with the ultraviolet absorption spectrum, a maximum is observed between 240 and 250 mμ. The maximum at 240 to 245 mμ with the ultraviolet spectrum would be expected since it represents a Δ^4-3 keto grouping on the compound.

There appears to be relatively little difference in the ability to penetrate into the aqueous humor between the three compounds investigated although it appears from the absorption curves that topical application of the steroids achieved a slightly greater penetration into the aqueous humor than when administered systemically.

Summary

The chromatographic separation of eluates of pooled aqueous humor from animals treated with Medrol (free alcohol), Decadron and Kenacort both systemically and topically revealed a concentration of between 1.0 and 1.5 μg. of steroid per 1.5 ml. of pooled aqueous humor. Subsequent ultraviolet and sulfuric acid chromagen absorption spectrums substantiated the presence of the compounds by comparison to known standards.

1601 Spring Garden Street (30).

References

1. Burton, R. B., Zaffaroni, A., and Keutmann, A.: Paper chromatography of steroids: II. Corticosteroid and related compounds. J. Biol. Chem., **188**:763, 1951.

2. Green, H., Kroman, H. S., and Leopold, I. H.: Corticosteroids in the aqueous humor of the rabbit. AMA Arch. Ophth., **54**:853, 1955.

3. Green, H., Sawyer, J. L., and Leopold, I. H.: Investigation of corticosteroids in the aqueous humor of normal rabbit eyes. Am. J. Ophth., **39**:871, 1955.

4. Leopold, I. H., and Kroman, H. S.: Concentration of methyl and fluoro substituted prednisolones in the aqueous humor and blood of the rabbit. In press.
5. Pechet, M. M.: Methods with a chromatographic separation of very polar steroids. Science, **121**:39, 1955.

BINOCULAR VISION IN UNILATERAL APHAKIA*

Corrected by the Strampelli lens

C. Maggi, M.D.
Rome, Italy

The problem of full functional recovery in unilateral aphakia has always been of great importance, though only recently has it come to be considered in clinical practice.

There has already been much interest in contact lenses, as shown by the numerous publications on the subject. Town, Girandel and Maione expressed a favorable opinion, though their statistics were limited. Hirtenstein demonstrated 18 cases (11 were traumatic), only two of which were unsuccessful; however, all cases were chosen as being particularly favorable, with absence of squint, of comparatively recent onset (maximum of three years since the lesion); the youngest patient was 13 years of age, most were between 20 and 40 years of age. Cross has published accurate research showing that only four percent of all contact lens wearers are aphakic, and that only slightly more than half of these persevere with use of the contact lens.

Founding of a contact lens department at Moorfields Eye Hospital, London, has allowed ample and detailed study of the problem. The publications of Lyle and Ridley show that it is possible to maintain binocular vision only if the duration of suppression of the eye concerned is not protracted. As the corneoscleral type of lens is used, the patient must also wear a contact lens in the unaffected eye, in order to prevent the vertical deviation which would otherwise result, owing to the mechanical limitation of the eye wearing the lens. Only 50 percent of these patients with unilateral aphakia enjoyed binocular vision after a certain time, owing to lack of perseverance in use of the lens.

In the United States the results seem more encouraging, perhaps better tolerability of the contact lenses (corneal type, sometimes lacrilens) accounts for this. Goar obtained binocular vision in a large percentage of his cases. Constantine and McLean failed to get fusion in only five of 30 cases; of the 25 successful cases 14 needed training with prisms and binocularity was eventually attained. These authors seemed optimistic and held that binocular vision could be gained even in cases with uniocular aphakia and squint, when treated with contact lens and prism training.

Salvatori obtained orthophoria in 60 out of 62 cases, in six of them after training with prisms.

With the use of the Strampelli anterior chamber lens and the consequent ease of discission, binocular vision became even more easily obtainable. Barraquer, in his extensive statistics, almost always obtained fusion, as did Bietti and Apollonio, who have published successful results.

Choyce has reported on 60 cases operated by the Strampelli method, of which 20 were traumatic; binocular vision resulted in almost all the cases, if it had existed previously. However, in cases of protracted optical occlusion of an eye almost always there was eventual alternating suppression without diplopia. According to Barthelmeiss, using the

* From the Ophthalmological Department of the Hospital of S. Giovanni, Rome, directed by Prof. Benedetto Strampelli, to whom I am indebted for permission to publish these cases operated by him.

Schreck lens, the length of the functional exclusion had no importance whatever in the attainment of binocular vision, the conditioning factors being, on one hand, the sensorial conditions or absence of amblyopia and a sufficient visual acuity and, on the other, absence of muscular deviation or torsion. This author, however, obtained spontaneous binocular vision in only 10 percent of his cases.

In America, Reese and Hamdi believed that perfect stereopsis could be reobtained, as in one case of their large statistics. Schusterman and Harshman, using the Ridley lens, found that binocular vision resulted whenever definite good vision was attained. Lieb and Guerry reported failure in the establishment of binocularity in only three of their 29 cases. In six of them squint persisted after the lens implant in the anterior chamber and binocular vision was gained by means of orthoptic training. Stereopsis was attained only in the cases with eventual perfect visual acuity, and with some delay.

The statistics presented here have been analyzed with the object of evaluating the advantages and limitations of the Strampelli method, which has been used in this hospital since 1955, to attain binocular vision. For this reason, those cases are excluded in which there was primary amblyopia, cases still under treatment, or awaiting operation either for secondary cataract or for squint, and those in which the aphakia is bilateral, or in which cataract has subsequently developed in the other eye.

In all 32 cases are presented here. The type of lens used in 29 of them is the classical triangular one, and in the other three, the new type, a round lens suspended by two acrylic threads anchored under the conjunctiva. Normal visual acuity was obtained in 17 cases (representing 53.12 percent of the total), and in only eight cases remained below 5/10. Binocular vision was established immediately in 17 cases, and after a period varying from two to 18 months in nine other cases; in seven of these orthoptic treatment was of help. In only six cases was binocular vision not obtained (fig. 1).

In nine cases, although a reasonable visual acuity was obtained with introduction of the lens, binocular vision did not occur immediately, owing to the presence of suppression (represented in Figure 1 by a triangle in which the ascending line indicates the gradual disappearance of the suppression, terminating in the acquisition of binocular vision).

The reason for this suppression seems to lie in the difficulty the patient experiences in using the affected eye, due to the lack of accommodation, and the delay in restoration of binocular vision is present in patients who have had cataracts for the longest period, as binocular vision had been inhibited for a longer time.

Binocular vision was restored in all the nontraumatic cases, even when, as in Case 11, the exclusion by cataract lasted 12 years. This may be due to the more advanced age of the patient at the time of onset, and perhaps also to the slow onset of the optical obstacle in these cases.

The traumatic cases are, however, mainly in children or young persons, in whom the exclusion of an eye occurs abruptly, and it appears that in these cases the suppression is profound, and again conditioned partly by the duration of the unilateral occlusion. Furthermore the relationship between the duration of the cataract and the depth of suppression is more evident the younger the patient. In other words the duration of the cataract becomes more threatening to the conservation of binocular vision in younger patients.

The delay in the restoration of binocular vision, present in only two nontraumatic cases, may be seen in seven of the traumatic cases. Could it be assumed that some of the seven cases of delayed binocular vision after traumatic cataracts would not have recovered binocularity if treated by contact lenses instead of intraocular ones?

In the six cases in which binocular vision was not obtained, the most obvious reason seems to be the limited visual acuity; in all of them it was below 4/10. This tallies with the findings of Spaeth, who demonstrated

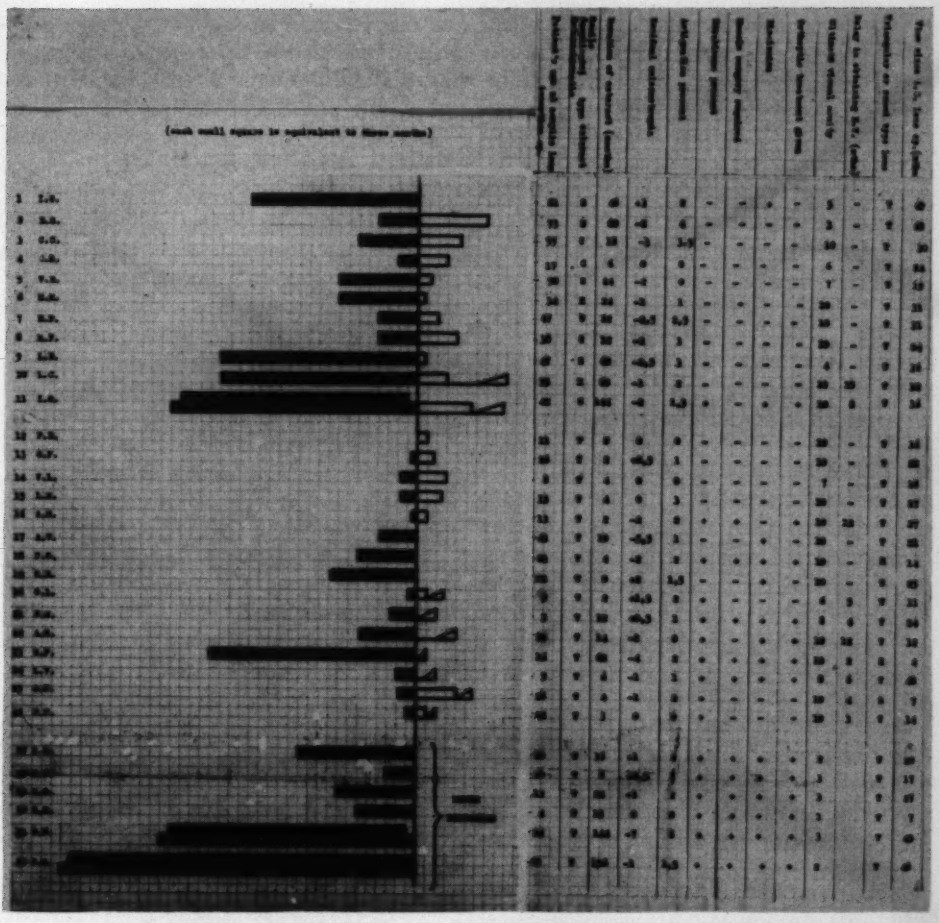


Fig. 1 (Maggi). Cases 1 to 11, nontraumatic cataracts with binocular single vision. Cases 12 to 26, traumatic cataracts with binocular single vision. Cases 27 to 32, traumatic cataracts without binocular single vision. The central vertical line represents the moment when the inhibition was removed, that is, the time of the operation of cataract or of discission. The initial shaded portion indicates the actual duration of the visual inhibition due to the presence of cataract. The blank portion after operation represents the duration of aphakia, terminated by the introduction of the anterior chamber lens, and the attainment of binocular vision. In many cases there is no interval of aphakia and binocular vision is obtained immediately after the cataract operation, as the lens is introduced simultaneously, as in Case 1. This also occurs frequently in traumatic cases, in which, in order to prevent loss of vitreous, the lens is introduced first, followed by discission.

suppression whenever the visual acuity was less than 3/10. In four of these cases the visual deficiency was attributable to a persistent secondary cataract which was resistant to surgery, causing amblyopia in one case.

In the last two cases in Figure 1, lack of fusion rather than low visual acuity seems responsible, as both cases had had cataracts for many years during the very period when the fusion faculty should have been consolidated; in fact, although there was deep suppression under normal conditions, diplopia could always be elicited at the synoptophore, with variable hyperphoria, and in spite of orthoptic training, fusion could not be developed.

Muscular deviation, which seems to be the final consequence of a state of suppression, was present in all cases with delayed binocularity. If the delay is particularly prolonged there is a progressive increase in the angle of deviation, until, in some cases, surgery becomes necessary, if the deviation becomes an obstacle to binocularity (Cases 21, 23 and 24). In most cases removal of the suppression results in spontaneous disappearance of the deviation (as in Cases 25 and 26, where corneal precipitates cleared in a few weeks).

This deviation in all our cases was of the excess-of-divergence type and the recovery of binocular vision for near was also gradually followed by recovery for distance, sometimes leaving a residual exophoria. This excess of divergence was thought to be due to the fact that the focus of the operated eye is fixed. For the near position (with the reading correction) the patient can select his own near-point of clear vision for the aphakic eye and adapt the normal eye to that distance but, outside this range, active accommodation of the operated eye is of course nonexistent, and blurred vision and macular suppression result, giving rise to excess of divergence. For this same reason it is advisable to prescribe occlusion of the normal eye for a short period immediately after the operation so that the patient can adapt himself to the correct working distance for the aphakic eye and to adapt the other eye to this focusing distance.

In young children the presence of hypermetropia and the ample reserve of accommodation tend to cause convergent squint in the presence of unilateral suppression (as in Case 30). Once a convergent squint has developed under these conditions, it may be overcome only with difficulty, even surgically.

Residual myopic anisometropia is intentional, with the scope of reducing the spherical positive correction for close work in the aphakic eye, and of minimizing the inevitable aniseikonia for both near and distance positions. However, the aniseikonia was never distressing, neither were there any symptoms of eye strain.

Most authors hold that binocular vision can be restored after operation only when it existed immediately beforehand, though we have found that even when binocularity existed only in the first few years of life full fusion could be restored after operation, as in Case 17, who at the age of 43 years developed a traumatic cataract in his emmetropic eye, the other eye having been myopic (9.0D. sph.) for as long as he could remember. In order to restore full binocular vision with stereopsis it was sufficient to render the aphakic eye myopic to the power of 4.0D. sph.

Normally, preoperative absence of deviation and the presence of normal retinal correspondence are sufficient to indicate that binocular vision can be restored after introduction of the lens, irrespective of the time lapse. However, in cases in which an insuperable anisometropia occurs in the first few years of life with a sudden onset instead of a gradual one (as in the case of traumatic cataract as opposed to unilateral myopia), amblyopia occurs, unless all surgery (cataract extraction, introduction of lens, discission if necessary) is performed within a short period. If the cataract occurs later (though still before the age of six or seven years) and the patient remains untreated for many years, binocular vision will probably be lost (as in Cases 31 and 32), even if fair vision in the aphakic eye is retained.

Conclusion

Binocular vision was obtained in 81 percent of our cases; the recovery was spontaneous in 61.4 percent of these.

In cases of nontraumatic origin there was recovery of binocular vision in 100 percent of the cases.

In unilateral traumatic aphakia a profound suppression of the affected eye occurs, being correspondingly more intense the younger the patient and the longer the duration of the cataract.

The rapidity of treatment (the operation of cataract, the lens introduction and discision) is of fundamental importance for a good functional result.

The corneal contact lens, though useful in

many cases, can be insufficient whenever the tendency to suppression is such as to require a continual stimulation of the binocular vision, which may only be given by the intraocular lens. The latest type of Strampelli disc-shaped lens may be preferred for ease of introduction and subsequent discission.

Via Pistoia 19.

References

1. Apollonio: Lenti acriliche fisse in camera anteriore. Boll. Ocul., **35**:114, 1956.
2. Barraquer and Bailbè: Incidents, accidents et complications possibles au cours de l'inclusion de lentilles plastiques dans la C. A. Bull. Soc. Franç ophtal., **70**:233, 1957.
3. Barthelmess: Der binocularen Schalkt nach Implantation von Vorderkammerlinsen. Ber. deutsch. ophth. Gesalt., **60**:137, 1956.
4. Bietti: The present state of the use of the plastics in eye surgery. Acta Ophth., **33**:337, 1955.
5. Constantine and McLean: Contact lenses in aphakia. Arch. Ophth., **51**:212, 1954.
6. Choyce: Correction of uniocular aphakia by means of anterior-chamber acrylic implants. Tr. Ophth. Soc. U. Kingdom, **58**:459, 1958.
7. Cross: Contact lenses: An analysis of the results of use. Brit. J. Ophth., **33**:421, 1949.
8. Girardet: Verres de contact et aphakia. Ophthalmologica, **116**:226, 1948.
9. Goar: The management of monocular cataracts. Arch. Ophth., **54**:73, 1955.
10. Hirtenstein: Contact lens in unilateral aphakia. Brit. J. Ophth., **34**:668, 1950.
11. Lyle, T. K.: The importance of orthoptic investigation before contact lens fitting in unilateral aphakia in a preliminary report. Tr. Ophth. Soc. U. Kingdom, **73**:387, 1953.
12. Maione: Vetri di contatto e afachia. Ann. oftal., **75**:127, 1949.
13. Paufique: Operation de Ridley. Bull. Soc. Franç ophtal., **67**:378, 1954.
14. Ridley, F.: Contact lenses in unilateral aphakia. Tr. Ophth. Soc. U. Kingdom, **73**:373, 1953.
15. Rougier: La correction de l'aphakia unilaterale par les verres de contact et par les lentilles cristalliniennes de Ridley. Etude comparative. Bull. Soc. Franç ophtal., **67**: 391, 1954.
16. Schusterman and Horshman: Plastic lens insertion after cataract extraction. Tr. Canadian Ophth. Soc., **9**:108, 1957.
17. Spaeth: The treatment of monocular aphakia. Trans. Ophth. Soc. U. Kingdom, **77**:517, 1957.
18. Strampelli: Sopportabilità di lenti acriliche in camera anteriore nella afachia e nei vizi di refrazione. Atti Soc. Oftal. Lombarda, 1953, p. 292.
19. ———: Complicatios de l'operation de Strampelli. Année therapeutique et clinique en Ophthalmologie, 1958, Tome IX, p. 349.
20. ———: Recenti orientamenti nell'impianto di lenti in camera anteriore. Ann. Ottal. & Clin. Ocul., **85**:361, 1959.
21. Town: Contact glasses for correction of refractive errors in monocular aphakia. Production of binocular vision. Arch. Ophth., **21**:1021, 1939.
22. Ogle, K., Burian, H., and Bannon, R.: On the correction of unilateral aphakia with contact lenses. Arch. Ophth., **59**:639, 1958.
23. Reese, A., and Hamdi: Five years' experience with the Ridley operation. Arch. Ophth., **58**:389, 1957.
24. Lieb, W., and Guerry, D.: Experiences with an anterior chamber lens. Am. J. Ophth., **46**:127, 1958.

OPHTHALMODYNAMOMETRY: A PILOT STUDY*

Jerome Frankel, M.D.

Columbia, Missouri

The appearance of a spontaneous retinal arterial pulse was first noted and recorded by Donders over 100 years ago. Arterial pulsations of a spontaneous nature may be seen in glaucoma, and may be noted in the central retinal artery when finger pressure is applied to the globe.

Bailliart, in 1917, devised a simple standardized tension spring instrument called the ophthalmodynamometer and used it for applying and recording increasing pressure

* From the Department of Ophthalmology, Michael Reese Hospital, Chicago. This study was supported by the Charlotte Rosenbaum Grant for Ophthalmic Research. Presented before the Chicago Ophthalmic Society, May 16, 1960.

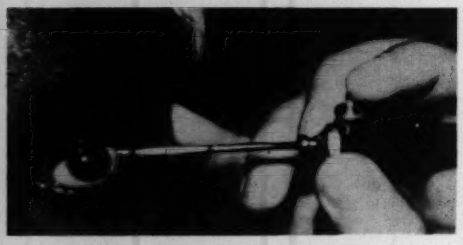


Fig. 1 (Frankel). Picture of Bailliart's ophthalmodynamometer.

upon the eye. The enthusiasm, both for the instrument and technique for determining carotid artery pressures, was short-lived in the 1920's and 1930's. This was the result of the literature, here and abroad, which was overly concerned with attempts to prove absolute values for retinal artery pressures and rigid ratios between these and systemic blood pressures. Values for these could not be agreed upon and it was pointed out that readings of retinal pressure would be variable and influenced by factors such as scleral rigidity, globe size, and intraocular pressure.

It has only been in recent years that the ophthalmodynamometer has been recognized as an aid in cerebrovascular diseases. This has resulted from the recognition of the technique as a value in comparative and relative measurements between the two eyes of the same individual.

The rationale of ophthalmodynamometry in the diagnosis of carotid artery disease is based on observations from experiments that occlusions or insufficiencies of the carotid artery will usually cause lowering of the blood pressure in its first branch, the ophthalmic artery, and in the central retinal artery. A lowered pressure in one retinal artery may well indicate internal carotid embarrassment on that side.[13]

Why has this become so important? First, it has been estimated that one third of all patients who enter a hospital with the diagnosis of "stroke" or cerebrovascular accident are subsequently found to have diseases of their carotid arteries, that is, insufficiencies or thromboses. Second, most such insufficiencies can be treated more adequately either surgically or medically if the diagnosis is made promptly.

Smith and his co-workers[10] feel that retinal artery pressures should be done in any clinical evaluation of cerebrovascular accidents (including strokes due to carotid disease, pulseless disease, aortic arch syndrome, and basilar artery insufficiency). It should also be used to evaluate cases of amaurosis fugax, and to evaluate anticoagulant or surgical therapy such as carotid ligations and endarterectomies.

Spalter,[12] in his investigations, clearly shows that the signs and symptoms of carotid artery disease are extremely variable. He divides his study of 50 positive cases into three main groups. Table 1 shows the natural history of carotid artery disease.

Amaurosis fugax is the most characteristic

TABLE 1

NATURAL HISTORY OF CAROTID ARTERY DISEASE

Acute Episodes (35% Incidence)	Transient Episodes (40% Incidence)	Slowly Progressive Course (25% Incidence)
a. Sudden onset without warning	a. Lasts minutes to several hours	a. Simulates brain tumor
b. Identical to severe stroke clinically	b. Frequency variable	b. Increasing paresis, psychic disturbance, field loss
c. Loss of consciousness, hemiplegia, aphasia	c. Symptom complex also reproducible	c. Course may be interrupted by development of collaterals
d. May simultaneously thrombose ophthalmic artery	d. Intermittent paresis, aphasias, amaurosis, sensory loss	
e. Mortality 35%	e. Normal periods between episodes	

symptom of carotid artery disease. It cannot merely be explained on the basis of occlusion of the ipsilateral internal carotid artery since it has been shown by Schimek and Beallo and others[9] that if one occludes the internal carotid on one side, the ophthalmic artery on the same side fills by way of collaterals from the external carotid artery. In some instances the collaterals are from the opposite external carotid (fig. 2). Collateral filling from the opposite side has also been demonstrated through the circle of Willis by dye studies and arteriography.

The most attractive theory, then, for transient blindness is not occlusion per se but rather transient falls in systemic blood pressure superimposed upon an already compromised circulation. The decreased blood pressure can be caused by postural change, emotional stress, or a variety of other causes.

Other characteristics of the disease not as frequent as amaurosis fugax, such as cotton-wool patches in the retina or unequal hypertensive changes, are seen in less than 20 percent of the positive cases. Bruits are found in less than two percent of the cases and conjunctival blood vessel changes have been reported by only one group and not confirmed by others.

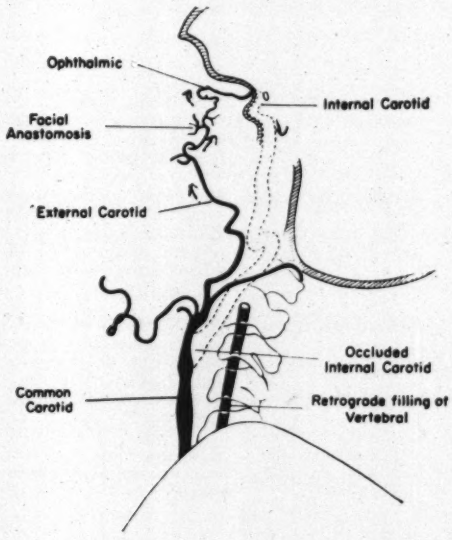


Fig. 2 (Frankel). Diagrammatic representation of collateral circulation in carotid artery obstruction. (From Schimek and Beallo.[9])

TABLE 2

PERCENT OF DIFFERENCE IN RETINAL ARTERY PRESSURE IN 49 NORMAL INDIVIDUALS

Percent	Persons	Total Percent
0– 5	26	52
6–10	12	26
11–15	8	16
16–20	2	4
22	1	2

PRESENT STUDY

In the present investigation, 50 normal subjects were chosen at random from the Michael Reese Hospital service and eye clinics. No patients with a history of glaucoma, retinal disease, very high myopia, or previous eye surgery were included in the sampling. Examination was done with the patient in a sitting position, after the eyes were anesthetized with topical ophthaine. Where needed, paredrine (one percent) was used topically to dilate the pupil.

All determinations were repeated three times on each eye and an average of these was taken. This was necessary since factors such as corneal or media haziness and high corneal astigmatism make accurate end-points more difficult to obtain. Variations in readings may also be caused by cardiac irregularities.

The pressure percentage difference between eyes was calculated by a simple formula presented by Spalter and may be used either for diastolic or systolic pressures. This formula for retinal artery pressure (R.A.P.) difference is:

$$\frac{\text{Higher R.A.P.} - \text{Lower R.A.P.}}{\text{Higher R.A.P.}} = \text{Percent difference}$$

Some investigators[6,12] record only diastolic pressures and consider them most accurate and reproducible while others do systolic pressures routinely. In doing systolic pres-

TABLE 3

TEN CASES WITH NONSPECIFIC CEREBRAL COMPLAINTS

Patient	Age (yr.)	Sex, Race	Case History—Salient Facts	R.A.P.* Difference (%)	Diagnostic Impression	Evidence
L. B.	58	C/F	Blackouts, 6 wk.; personality change; petit mal attacks, recent	4	Suspect small cerebrovascular accident or idiopathic epilepsy	Normal EEG, arteriography, ventriculography, and visual tests including fields
S. M.	67	C/M	Recent persistent headaches; episodes of ataxia, 1 mo.	0	Posterior cerebral artery insufficiency	Positive arteriogram, homonymous quadrantic field defect, normal arteriogram for carotids
R. G.	65	W/F	Frequent blackouts, 2 mo.; occasional sudden weakness, left leg	15	Cerebral arteriosclerosis with vasospastic episodes	Skull films: right parietal calcifications and a long superior saggital suture; arteriorgrams normal
B. J.	62	C/M	Sudden personality change—disoriented, withdrawn, confused	9	Probable right cerebral artery thrombosis	Fields: left homonymous hemianopsia with macular sparing; skull x-ray normal; arteriogram refused
F. S.	28	C/F	Sudden progressive right arm paresis; slurred speech, recent; comatose state; sluggish pupillary reaction	8	Left subdural hematoma	Skull films: ventriculography suggestive; craniotomy showed clot
J. G.	54	W/F	Intermittent occipital headaches, 6 da. duration; weakness of right upper arm; defect in recognition of objects; ptosis, right eye; semistuporous; positive Babinski and Chaddock on right side	16	Left subdural hematoma	Arteriogram: anterior cerebral artery pushed to right side; craniotomy showed blood clot
A. T.	39	W/M	Progressive proptosis o.s., 6 mo.; transient diplopia since 2 wk. P.T.A.	0	Left subdural hematoma	Arteriogram: anterior cerebral artery pushed to right side; craniotomy showed blood clot
H. S.	50	C/F	Paresthesia, both upper extremities; vertigo and headaches; polyuria, polydypsia	0	Pituitary adenoma	Skull films: enlargement and erosion of floor of sella tursica with extension to sphenoid sinus; peripheral fields suggestive on right side
J. P.	23	W/F	Intermittent blurred vision of right eye, 2 wk.; horizontal nystagmus on lateral field gaze; recent intermittent episodes of vertigo, ataxia	5	Multiple sclerosis	Normal skull, c.s.f. and acoustic tests; age group, multiplicity of unrelated symptoms later improved; persistent enlarged blind spot o.u. (15×20)
B. L.	58	W/M	Intermittent blurred vision O.U.; several weeks; slurred speech, vertigo, agraphia, asterognosis	3	Metastatic bronchogenic carcinoma of brain	X-ray: positive chest and brain; postmortem examination

* R.A.P., Retinal artery pressure.

TABLE 4

CASE WITH PROBABLE CAROTID DISEASE

Patient	Age (yr.)	Sex, Race	Case History—Salient Facts	R.A.P.* Difference (%)	Diagnostic Impression	Evidence
B. N.	65	W/F	Two transient episodes of complete blindness in the right eye lasting several seconds within the last month; episodes of left lower extremity weakness with a positive Babinski (recent); episodes of vertigo and slurred speech	40	Right carotid artery insufficiency	Pressure over area of right common carotid artery caused vertigo and slurred speech; patient debilitated, arteriogram not attempted; fields, fundi, acuity non-contributory

* R.A.P., Retinal artery pressure.

sures, there is a possibility of inducing permanent closure of the central retinal artery. Spalter[12] reported one such case with permanent visual impairment which was precipitated in a medical center where systolic pressure determinations were done routinely. Another case of transient occlusion of the central retinal artery occurred but subsided without permanent damage. For these reasons only diastolic determinations were done in this study. Patients whose retinal arterioles are rigid and sclerotic require a great deal of external pressure from the instrument before pulsating. The pressure may be great enough to cause a subconjunctival hemorrhage but this is rare and obviously of less consequence than closure of the central retinal artery.

An analysis of the 50 cases can be summarized as follows: The age range was eight to 85 years and half the group were between 50 to 69 years of age. The sex ratio was equal. The group was half white and half Negro. The ocular tension in each eye of every subject was under 25 and essentially equal. It was, therefore, unnecessary to change from gm. of pressure to mm. of mercury. Table 2 shows the results.

It can be seen that 94 percent of normal subjects had a central artery pressure difference of 15 percent or less. More than half were five percent or less. Two patients showed a 16 to 20 percent difference. The highest normal was 22 percent in a patient who was symptom free, the criterion for normalcy. His end-points were easy to read and were consistent each time.

It is generally agreed that consistent borderline differences, that is, 15 percent in the presence of neurologic symptoms, warrants an arteriogram. It is also agreed by most investigators that there is a certain amount of overlapping between normals and patients with obstructions of the carotid arteries. Usually there exists a 36 to 59 percent decrease in pressure on the occluded side, but in cases where the collateral is excellent no decrease in central retinal artery pressure will be found.

In a private hospital, ophthalmodynamometry finds its greatest usefulness in patients presenting with nonspecific cerebral symtomatology. It is a critical help to the internist and neurosurgeon as well as to the ophthalmologist in cases of diagnostic uncertainty.

Table 3 briefly summarizes 10 patients whose case histories suggested or hinted at carotid artery occlusion. The pathology subsequently proved to be another disease entity but notice how helpful the results of doing central retinal artery pressure proved to be in ruling out carotid artery occlusion. As Table 3 shows, the diagnoses were cerebrovascular accidents of other cerebral arteries, subdural hematomas (three), a pituitary adenoma, a case of probable multiple sclerosis, and a metastatic carcinoma to the brain.

In one study of a 65-year-old white woman, the case history pointed to a right internal carotid artery occlusion. As can be seen in Table 4, she had some characteristic symptoms. The retinal artery pressure of the right eye was 40 percent lower than that of the left eye. In addition, pressure over the area of the right common carotid artery caused a vivid reappearance of her symptoms of vertigo and slurred speech. Her complete eye examination was noncontributory, and unfortunately she was too debilitated by a generalized lymphoma to undergo angiography. If done, it most likely would have clinched the diagnosis of carotid artery occlusion.

Summary

The history and development of the ophthalmodynamometer are briefly discussed. The characteristics and natural history of carotid artery occlusion are described.

In the present study, the retinal artery pressures were determined on both eyes of 50 normal patients. The percent difference between the central artery pressures generally did not exceed 15 (94 percent of cases). Over half of the group had differences of less than five percent. The value of the technique with patients showing nonspecific cerebral symptomatology is discussed.

601 South Fifth Street.

References

1. Fisher, C. M.: Cranial bruit associated with occlusion of the internal carotid artery. Neurology, **7**: 299-306, 1957.
2. Gordon, N.: Ocular manifestations of internal carotid artery occlusion. Brit. J. Ophth., **43**:257-267, 1959.
3. Henderson, J. W., and Schneider, R. C.: Ocular findings in carotid cavernous fistula. Am. J. Ophth., **48**:585-596, 1959.
4. Heyman, A. J., Karp, H. R., and Bloor, B. M.: Determination of retinal artery pressures in diagnosis of carotid artery occlusion. Neurology, **7**:97-104, 1957.
5. Hollenhorst, R. W.: Ocular manifestations of insufficiency or thrombosis of the internal carotid artery. Tr. Am. Ophth. Soc., **56**:474-506, 1958.
6. ———: Ophthalmodynamometry and intracranial vascular disease. Med. Clin. North Am., **42**:951-958, 1958.
7. Pavlou, A. T., and Wolff, H. G.: Conjunctival vessels in carotid artery occlusion. AMA Arch. Int. Med., **104**:53-60, 1959.
8. Perry, R. B., and Rose, J. C.: Ophthalmodynamometry. Circulation, **18**:864-870, 1958.
9. Schimek, R. A., and Beallo, A.: Ophthalmodynamometry. Am. J. Ophth., **48**:220-228, 1959.
10. Smith, J. L., et al.: Ophthalmodynamometric diagnosis. J.A.M.A., **170**:1403-1407, 1959.
11. Smith, J. L., and Cogan, D. G.: Ophthalmodynamometric posture test. Am. J. Ophth., **48**:735-740, 1959.
12. Spalter, H. F.: Ophthalmodynamometry. Am. J. Ophth., **47**:453-467, 1959.
13. Svien, H. J., and Hollenhorst, R. W.: Retinal artery pressures after ligation of the carotid artery. Proc. Staff Meet. Mayo Clin., **31**:684-692, 1956.
14. Van Allen, et al.: Retinal artery pressure measurements in diagnosis and surgery of spontaneous carotid occlusion. J. Neurosurgery, **15**:19-24, 1958.
15. Wood, A., and Toole, J. F.: Ophthalmodynamometry. J.A.M.A., **165**:1264-1270, 1957.

Ophthalmic Miniature

A New York oculist claims to have discovered a disease of the eye characterized by a dimness and "a film-like gathering" over the eye, which he traces directly to cigarette smoking. He calls it the "Cigarette Eye."

The Medical Record, **35**:100, 1889.

STUDIES ON THE HEALING OF CORNEAL GRAFTS*

II. The fate of the endothelial cells of the graft as determined by sex chromatin studies

Romeo B. Espiritu, M.D., Gerald B. Kara, M.D., and David Tabowitz, B.A.
New York

The importance of a normal endothelium in corneal healing, whether it be a cataract incision or a penetrating graft, as well as in the maintenance of corneal transparency, has always been emphasized. In corneal surgery great care is always taken not to damage the endothelium unduly. A graft with its epithelium scraped off will still heal satisfactorily, but this is not the case if the endothelium is damaged.

Role of the endothelium in corneal healing

It is known that mitoses are very rarely seen, if ever, in the endothelial layer under normal conditions. The endothelial cells divide by amitosis. The process of endothelial repair in corneal wounds has been the subject of recent studies. Binder and Binder,[1] by denuding the posterior corneal surface of one portion of the endothelial cells, have shown that the involved area begins to be surrounded by active cells with pseudopodiumlike processes within 12 hours and mitotic and amitotic figures appear. The defect is completely covered by endothelial cells in four days. They believe that the new cells come from the surrounding endothelium. Similar findings were reported by Chi, et al.[2] Stocker,[3] on the other hand, in a histopathologic study of the endothelial repair in corneal wounds, has suggested that the new cells arise from the corneal fibroblasts. Dunnington[4] agrees with this latter view. Morton, et al.[5] found complete endothelial healing of corneal wounds, made with a discission needle introduced into the anterior chamber, in 48 hours but the cells continued to proliferate, forming a fusiform scar not unlike fibrous tissue in appearance. The difference in the findings, however, may depend on whether or not Descemet's membrane is intact. If Descemet's membrane is injured, the stroma cells participate in the healing process.

The present study was undertaken to investigate endothelial healing in corneal grafts. The problem dealt with was the eventual fate of the endothelial cells of the graft rather than the actual cellular origin of the endothelial cell.

Sex chromatin as a biologic marker

Tagging the cells to determine their fate in transplantation presented a problem in the past. The discovery of sex chromatin by Barr and Bertram[6] opened up new avenues of research not only in the determination of the genetic sex at the cellular level but it also provided the ideal biologic marker needed in transplantation studies. This is probably a much better method than the use of radioisotopes to tag cells, since the labeled element in the cell is less permanent and the duration of study is limited by the biologic half-life of the radioactive element.

The sex chromatin appears as a small hemispherical mass with its flat surface lying against the nuclear membrane. This is seen only in the cells of the female. The simplest explanation so far which accounts for this special body is that it consists of an XX pair of chromosomes which in combination are of sufficient size to be distinct from the rest of the chromatin, unlike the sex chromatin in the male in which the Y chromosome is too small to render the XY pair of chromosomes distinctly visible.

* From the Research Department, New York Eye and Ear Infirmary.

Fig. 1a (Espiritu, Kara and Tabowitz). Flat mount of female endothelium. Note female sex chromatin material (arrow). (×2,000, Thionin stain.)

Fig. 1b (Espiritu, Kara and Tabowitz). Flat mount of male endothelium. Note absence of sex chromatin material. (×2,000, Thionin stain.)

Pedler and Ashton[7] have shown that the sex chromatins are also demonstrable in ocular tissues, such as the conjunctival and corneal epithelium, stromal cells of the iris, epithelium of the ciliary processes, stromal cells of the ciliary body and the ganglion and nuclear cells of the retina. Basu and Ormsby[8] by the use of cultures have demonstrated the sex chromatin in the stromal cells of the cornea and have used this method in determining the fate of the stromal cells in corneal transplants.[9] Using the sex chromatin as a biologic marker, this present study was made to determine the fate of the endothelial cells of the graft.

Method

Penetrating keratoplasties were performed with a 6.0-mm. trephine on albino rabbits weighing 2.0 to 2.4 kg. under paraldehyde-demeral and topical Sympocaine (0.75 percent) (aminobutoxybenzoyldiethylaminoethanol HCl) anesthesia. The grafts were taken fresh from albino rabbits of the opposite sex. Great care was taken not to traumatize the endothelial surface of the graft, 7-0 interrupted silk sutures were used and the lids were closed with 4-0 silk sutures. Daily dressings were applied with atropine (one percent) drops and Neosporin ophthalmic ointment. The sutures were removed under anesthesia on the 10th day. The corneas were removed at various intervals after operation and flat mounts were made of Descemet's membrane and endothelium of the graft and host for sex chromatin studies. Only those grafts which were clear up to the time of the removal were studied.

Preparation of the flat mounts

The technique advocated by Stocker, et al.[10] was used in removing Descemet's membrane with the endothelium. As Descemet's membrane is firmly attached to the borders of the graft where scar tissue has formed, a continuous membrane could not be taken. The graft was excised first by means of a smaller trephine (5.0 or 5.5 mm.). The peeled-off Descemet's membrane of the graft and the rest of the surrounding host cornea were placed on a gelatin-coated glass slide.

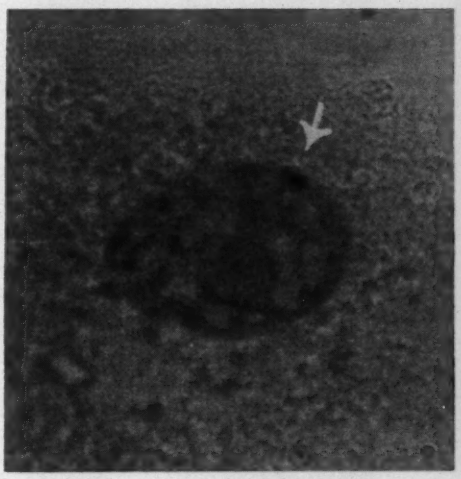


Fig. 2 (Espiritu, Kara and Tabowitz). Female endothelial cell obtained by tissue culture. Note female sex chromatin material (arrow). (×2000, Thionin stain.)

To eliminate the formation of artefacts which may be mistaken for sex chromatin, Descemet's membrane with endothelium was fixed immediately it was peeled off from the cornea for three hours in modified Davidson's solution. This procedure also makes it easier to prepare flat mounts, as Descemet's membrane, which has a tendency to curl up, can be flattened out easily over the slide after fixation. All procedures were done under a dissection microscope.

The procedure resulted in a monolayer preparation of endothelial cells. Of the different stains recommended for demonstration of the sex chromatin (Fuelgen,[6] hematoxylin,[11,12] Thionine,[13] Biebrich scarlet and fast green[14]) we found that Thionine (Ciba) gave the best over-all result: sharper differentiation of the sex chromatin from the nucleoplasm, deeper color and sharper nuclear detail. In addition, Descemet's membrane took up a negligible amount of the stain so that it did not interfere with the cellular visibility unlike some of the other stains (figs. 1a and

TABLE 1

SEX CHROMATIN COUNTS IN THE GRAFT AND HOST ENDOTHELIUM

Age of Graft	Sex		% Sex Chromatin		% Graft Cells Retained
	Graft	Host	Graft	Host	
1 wk.	Female	Male	89	2	89
2 wk.	Female	Male	96	4	96
3 wk.	Male	Female	5	93	95
	Female	Male	94	4	94
1 mo.	Male	Female	3	94	97
1½ mo.	Female	Male	87	4	87
2 mo.	Female	Male	81	8	81
	Male	Female	12	94	88
	Female	Male	81	6	81
3 mo.	Female	Male	83	7	83
4 mo.	Male	Female	13	94	87
	Male	Female	39	91	61
5 mo.	Female	Male	38	9	38
7 mo.	Male	Female	89	91	11

1b). With culture the proliferating endothelial cells still maintained their sex chromatins (fig. 2).

A percentage count was made of the sex chromatins in both the graft and host cells. A careful examination of the male cells was done as some occasionally show structures which resemble sex chromatin, such as indentations of the nuclear membrane or coarse particles of chromatin. Counts were made at various areas at the periphery as well as the center of the graft. A total of 300 to 400 cells on each slide were counted.

RESULTS

Control studies of preparations from normal female rabbit corneas revealed a percentage count of sex chromatin of 85 to 95 percent. The percentages of nuclei revealing identifiable sex chromatin as reported by different authors vary from as low as 30 percent to as high as 98 percent. Such variation may be explained by the method of obtaining the specimen, method of fixation, the type of stain used, the type of tissue and other variable factors. The high percentage count we got may be explained by the fact that the endothelium forms a single layer which could be placed undisturbed on flat mount preparations unlike other specimens prepared by scraping or sectioning wherein cutting off portions of the nuclei, distortion of the nuclei and overlapping of cells interfere with the count.

In Table 1, it will be seen that the endothelial cells of the graft retain their sex characteristics up to four months after operation when the percentage count drops down until at the seventh month almost all of the cells have assumed the sex characteristics of the host.

COMMENT

It appears that the endothelial cells of the graft persist for quite some time and perform their function of maintaining the transparency and normal physiology of the graft. However, after the fourth month, the cells eventually become replaced by those of the host until there is almost complete replacement by the seventh month. It is to be noted that such a change could not be due to physiologic death of the cells, as endothelial cells have a life span much longer than four months.

Binder and Binder,[1] in a study of amitotic and mitotic activity of the endothelial cells of the rabbit cornea, have calculated the life span of the cells to be around 344 days. It seems from our results that the endothelial cells have a more or less similar replacement period as that of stromal cells based on the study of Basu and Ormsby.[9] They have found that significant replacement of the cells did not occur until around three months after operation. A study by Kornblueth and Nelken,[15] using lamellar grafts in rabbits, has revealed that at no time was there any massive destruction of cells, suggesting that cells of the graft persist for some time.

Summary

The fate of the endothelial cells of the graft has been studied in rabbits using sex chromatin as a biologic marker. The cells in the graft persist for a period of four months. After this period the cells are replaced by those of the host and in seven months there is almost complete replacement with host cells.

218 Second Avenue (3).

Acknowledgment

We wish to acknowledge the invaluable technical assistance given by Miss Margaret G. Cubberly, B.S., H.T. (A.S.C.P.) on the histochemical and histopathologic studies. Miss Margaret G. Cubberly and Mr. John P. Goellar prepared the photographs.

References

1. Binder, R. F., and Binder, H. F.: Regenerative processes in the endothelium of the cornea. AMA Arch. Ophth., **57**:11-13, 1957.
2. Chi, H. H., Teng, C. C., and Katzin, H. M.: Healing processes in the mechanical denudation of the corneal endothelium. Am. J. Ophth., **49**:693-703, 1960.
3. Stocker, F. W.: The endothelium of the cornea and its clinical implications. Tr. Am. Ophth. Soc., **51**:669-786, 1953.
4. Dunnington, J. H.: Some modern concepts of ocular wound healing. AMA Arch. Ophth., **59**:315-323, 1958.
5. Morton, P. L., Ormsby, H. L., and Basu, P. K.: Healing of the endothelium and Descemet's membrane of rabbit cornea. Am. J. Ophth., **46**:63-67, 1958.
6. Barr, M. L., and Bertram, E. G.: A morphological distinction between neurons of the male and female and the behavior of the nucleolar satellite during accelerated nucleoprotein synthesis. Nature, London, **163**:676-677, 1949.
7. Pedler, C., and Ashton, N.: Sex of nuclei in ocular tissues. Brit. J. Ophth., **39**:362-367, 1955.
8. Basu, P. K., and Ormsby, H. L.: Identification of sex chromatin in corneal stromal cells for determination of the fate of corneal transplant. Transplantation Bull., **23**:435-436, 1959.
9. Basu, P. K., and Ormsby, H. L.: Sex chromatin as a biologic cell marker in the study of the fate of the corneal transplant. Am. J. Ophth., **49**:513-515, 1960.
10. Stocker, F. W., Eiring, A., Georgiade, R., and Georgiade, N.: A tissue culture technique for growing corneal epithelium, stromal and endothelial cells separately. Am. J. Ophth., **46**:294-298, 1958.
11. Moore, K. L., and Barr, M. L.: Morphology of the nerve cell nucleus in mammals with reference to the sex chromatin. J. Comp. Neurol., **98**:213-231, 1953.
12. Moore, K. L., and Barr, M. L.: Nuclear morphology according to sex in human tissues. Acta. Anat., **24**:197-208, 1954.
13. Klinger, H. P., and Ludwig, K. S.: A universal stain for the sex chromatin body. Stain Tech., **32**: 235-244, 1957.
14. Guard, H. R.: A new technique for differential staining of the sex chromatin and the determination of its incidence in exfoliated vaginal epithelial cells. Am. J. Path., **32**:145, 1958.
15. Kornblueth, W., and Nelken, E.: Partial lamellar corneal grafts in rabbits: Histologic observation on the survival of the stromal cells of the lamellar graft. Am. J. Ophth., **45**:242, 1958.

SOUTH AMERICAN OPHTHALMOLOGY RE-EXAMINED*

C. Dwight Townes, M.D., and Arthur H. Keeney, M.D.
Louisville, Kentucky

The late Dr. Moacyr E. Alvaro of São Paulo and the Pan-American Association of Ophthalmology have, since 1947, systematically arranged for North American and European lecturers to visit the medical centers of South America. In March and April, 1960, we were most pleased to complete such a tour to seven capital cities and were overwhelmed by the graciousness and warmth of these ophthalmic neighbors. This was the last lectureship to be arranged by Dr. Alvaro, but the association is planning to maintain such annual or semiannual visits. As is often the case, the visiting lecturer learns much more than he imparts. This report supplements that of Alan C. Woods ("South

* From the Section on Ophthalmology, the University of Louisville School of Medicine.

American Ophthalmology," Am. J. Ophth., 43:983-992 [June] 1957) following a similar visit to four South American universities in February, 1957.

Our itinerary covered Rio de Janeiro, São Paulo, Montevideo, Buenos Aires, Santiago, Lima, and Bogota, with mornings usually devoted to hospital and clinic rounds and afternoons to sightseeing, and evenings filled with banquets and lectures.

Brazil

The huge country of Brazil, with its giant cities of Rio de Janeiro and São Paulo, holds great opportunities for ophthalmology. Total socialization of medicine, however, has had tremendous impact, particularly on the career potential of young physicians. Every doctor is required to serve 24 hours each week in some government health agency. Generally this is accomplished by devoting mornings to such work and afternoons to private consultation. There are some "full-time" ophthalmologists on very low salaries who feel it is impossible for them to enter private practice.

Rio de Janeiro

In the federal District of Rio (similar to our District of Columbia) which existed until its transfer to Brazilia, April 21, 1960, there are about 225 ophthalmologists serving the 3.5 million population. The Universidade de Brazil, largest of the three medical schools in Rio, has 40 eye beds under the supervision of Prof. Werther Duque Estrada, a devoutly interested student of ophthalmology, who now holds the first chair of ophthalmology created in Brazil (1881). About 25 additional beds are available in the Institute Benjamin Constant in the large university center on Avenue Pasteur.

Residency training is extremely limited in Rio, as throughout South America, and the long-standing system of assistants or apprentices still is the fashion in local ophthalmic training. Most substantial ophthalmologists have had formal periods of training in Europe or the United States. A major interest of Brazilian ophthalmologists is surgical technique. Extreme degrees of finesse are cultivated and the exquisite fineness of many ophthalmic instruments from Spain and the Continent tend to make North American instruments seem heavy and gross.

Special eye hospitals have not been developed in Rio or São Paulo—in fact, only one exists in the entire country. The Brazilian Council of Ophthalmology has been organized along lines of our American Board of Ophthalmology and is slowly gaining strength in an effort to standardize ophthalmic qualifications on a higher level.

São Paulo

Sãa Paulo is the thriving industrial capital of South America and has two substantial medical schools. Escola Paulista, founded in 1933, is the smaller of these schools and was entirely private until 1956 when the federal government took over most of its support. It is here that the late Dr. Moacyr E. Alvaro held the Chair of Ophthalmology and fostered the international interchange in ophthalmology which brought many visitors to South America and widened the horizons of many northern hemisphere physicians. An efficient and modern Hospital São Paulo joins the old colonial courtyard buildings which are now devoted to administration. The eye clinic is well equipped and closely synchronized with the general teaching facilities. There are currently six full-time faculty members, including the dean. Tuition is $2.75 per year and classes are limited to 60 students.

Ophthalmology at Escola Paulista is coordinated with a unique "Centro de Estudos de Oftalmologia" founded by Dr. Alvaro in 1937 and located in a separate down-town building. An annual one-month refresher course and an annual postgraduate or basic science course covering an academic year are given in the Study Center; here also is the only school for orthoptists in South America. This covers an eight-month period. Lec-

ture rooms and an ophthalmic library supplement out-patient work in this Center. The large personal library of Dr. Alvaro is currently being combined with the resources of the Center to produce possibly the best eye library in South America.

The Universidade de São Paulo initiated its medical school in 1914 with Rockefeller aid and has now grown into a most cosmopolitan medical center of 1,700 beds and a heliport. In its principal Hospital das Clinicas, 35 beds are reserved for eye under the supervision of Prof. Cyro de Rezende and his faculty of 30 half-time ophthalmologists. Prof. Rezende, like his counterpart Prof. Duque Estrada in Rio, is greatly interested in corneal diseases and keratoplasty. Postgraduate ophthalmic training is developing and eight separate courses are outlined in the department publications.

Undergraduate teaching is in process of revision and consolidation. In keeping with suggestions at the First World Conference on Medical Education (London, 1953), Departments of Medicine and Surgery are being merged. Fifth year students receive 36 hours of ophthalmic instruction. The sixth year is being converted to a compulsory internship without formal courses or examinations.

These two schools and São Paulo itself throb with signs of rapid growth and expansion. Investigative ophthalmology will inevitably appear in such a complex. No visitor can leave São Paulo without an indelible, life-long impression of the 350-bed pemphigus hospital (Instituto Adhemar de Barros), constantly crowded with more than this number of chronic pemphigus foliaceus patients of all ages. Here Dr. Francisco Amendola, oculist to this institution, assembled the material for his prize-winning classic bilingual monograph "Manifestacões oculares do penfigo foliáceo" (São Paulo, 1947).

Montevideo

The buffer state of Uruguay, pinched between Brazil and Argentina, has only one medical school and this follows the six-year curriculum. Students generally average eight to 10 years before completion of their examinations. The freshman class averages about 600 students. All medical education is completely free and attendance at lectures is not compulsory. Licenses are automatically granted on graduation without further examination from any official extramural body. This is consistent with state-owned and operated education but removes one of the checks that North American education holds important in the surveillance of schools. Promotion in the various health services and university appointments require written examinations. Of the approximately 60 ophthalmologists in Uruguay, about 10 reside away from the capital city. Uruguay generally has better supply and distribution of physicians than most other South American nations.

Dr. Washington Isola, professor of ophthalmology, was, until recently, the Nation's Minister of Health and is well attuned to broad implications of medical training. Largely through the efforts of Dr. Isola, compulsory and free oral polio vaccine and oral BCG vaccine are given to all newborn infants. The university operates an unusual two-year course for certified ophthalmic assistants. Here about 12 girls pursue a two-year academic and practical course fitting them to do visual fields, assist in ocular surgery, handle orthoptics, and generally expedite the load of clinicians.

Montevideo, founded in 1726, is relatively a newer South American city and has been generally free of violent political unheavals. Maciel Hospital, built in 1750, is the oldest in the city and continues to occupy a blighted river-front site jammed to the sidewalk but still serving a useful mission. The new teaching Hospital de Clinicas is a striking 18-story building of contemporary design, but the upper nine floors have been unoccupied due to personnel shortages.

Buenos Aires

Argentine medicine has a great heritage through distinguished physicians but has suf-

fered enormous reverses through political upheavals, particularly the Peron period. Pedro Lagleyze, inventive surgeon and first professor of ophthalmology at Buenos Aires, the recently (1954) retired Prof. Arganarez, the retinal histologist Pio del Rio Hortega (1882-1945), the Nobel Prize physiologist Bernardo Houssay (1887-) and his distinguished son, and many others have made major contributions. The unique Hospital Oftalmologico Santa Lucia organized in 1878, still occupies a rambling quadrangle built in 1924 and is reminiscent of the Wills Hospital in Philadelphia. Unfortunately the urban grime that has darkened its stone work has also settled on the wonderful histologic and neurologic specimen museum of the late del Rio Hortega and his pupils. Emphasis on neuro-ophthalmology plus the assistance of three neurosurgeons here has led to incorporation of neurosurgery within the eye hospital—a unique and desirable wedding. At Santa Lucia, 54 ophthalmologists fill its 38 refracting lanes and tend the 600 to 900 patients seen on the Monday, Wednesday, and Friday clinic mornings. Surgery is scheduled on intervening mornings and commonly two or three cases are done in one operating room at the same time.

The other and younger eye hospital of Buenos Aires, Institute Pedro Lagleyze, was founded by Baudilio Courtis, incumbent professor of ophthalmology at the University of Buenos Aires. The Ministry of Social Assistance and Public Works maintains both these eye hospitals.

There are only two medical schools in Buenos Aires: one is a small and new Catholic school, and the other is the sprawling Universidad Nacional de Buenos Aires. Here the Evita Peron Foundation built a towering 15-story basic science building, and there is still under construction an adjoining 1,200-bed teaching hospital. The trend of socialized schools to have entering classes enlarged by government efforts favoring less fortunate candidates, brought the freshman medical class at Buenos Aires to 7,000 students under Peron. By gradual strengthening of entrance requirements the freshman class has now been reduced to 4,000 students and the faculty—in current difficulties of "reconstruction"—is aware of impossibilities posed by such masses of students. About 300 students graduate per year, but these are strung out commonly from one to five years beyond the prescribed seven curriculum years. Classrooms cannot accommodate the size of classes, examinations may be taken repeatedly, and the school's texts and microscopes are entirely free. Sincere efforts to develop modern education are hamstrung by strong student unions, looming faculty unions, and political factions. During our visit a strike of assistant and associate professors was in progress. One of the issues centered about the Medical Council of the University (commonly in our nation composed of the dean and department heads), which included two voting representatives of the student union, but no representatives of the part-time faculty.

The pleasant old Hospital de Clinicas (250 beds), again around attractive courtyards, has at least two statues of Pedro Lagleyze, the first professor of ophthalmology, and will continue to house the eye service until the new hospital is completed. Careful clinical forms are used on the service of Prof. Courtis, and some investigative work is being launched. There is less evidence of pride in current activities than in respect for accomplishments of the previous ophthalmic generation in their studies of histology, glaucoma and hereditary eye disease. A constant threat of uncertainty can be detected, however, even in casual conversations. Long-term, subordinate assistancies rather than residencies are still the rule of the day, but with nearly 300 ophthalmologists in this city of 3.5 million, there should develop a secure teaching and research program. The ingredients are certainly here; Dr. Courtis and his staff of 17 part-time faculty ophthal-

mologists are intent on developing a distinguished service.

Santiago

The University of Chile is the largest medical school of the three in this nation. The curriculum is seven years, with approximately 150 students in each class. Three general hospitals and two children's hospitals are utilized in the teaching program. The old Clinica Oftalmologica del Salvador was founded in 1925 by Prof. Carlos Charlin Correa (1885-1945) and his bronze bust graces the entrance of the high ceilinged old buildings. Currently Dr. Abraham Schweitzer is the soft-spoken and well-seasoned chief of staff, who, with 22 other ophthalmologists, keeps this 54-bed unit functioning harmoniously within the 1,000-bed Salvador Hospital complex. A beginning of clinical training is evidenced here by three young physicians on the house staff. The V Pan-American Congress of Ophthalmology which met in Santiago in 1956 had a medal struck in honor of Prof. Charlin C.; currently his son, Dr. Carlos Charlin V. follows in his famous father's footsteps, and edits the *Archivos Chilenos de Oftalmologia.*

Of the approximately 70 ophthalmologists in Chile, nearly all are in Santiago. Warm, familylike professional relations are fostered by Dr. Juan Verdaguer, the professor of ophthalmology. The fact that Dr. Herman Allesandri of the medical faculty is the brother of the president of Chile, and that both are setting distinguished courses, has brought pride and attention to the medical school. A fire in 1948 which destroyed the library and most of the school, has accelerated a magnificent long-range plan to create an ultramodern, earthquake proof plant. This is slowly being built on a pay-as-you-go plan. The hub of the plant will be a huge, round library and radiating from it will be academic, hospital, and research buildings. The Hospital Clinico (José Joaquin Aguirre) was completed in 1954 and the new anatomy building has been used for several years. Ten or more years will be required to bring the new plant into operation. This bids well, however, for thoughtful and proper growth of medical activity.

Lima

Medical fame came to Peru through skull trephination 500 years before Christ and more recently through its native rubiaceous trees whose bark was used in 1638 to treat malaria in the wife of Viceroy Cinchona. Now the Institute of Altitude Physiology brings credit to medical activities in Lima. The Peruvian capital boasts the oldest university in the Americas, Universidad Nacional Mayor de San Marcos, founded in 1551. Its Facultad de Medicina was organized in 1856, and its charming open quadrangle built in 1885. An ultramodern chemistry building has been opened and signs of growth are evident. Six hospitals are utilized for clinical teaching, including Peru's only children's hospital (Hospital del Nino, 500 beds, including 20 for eye, built in 1921) with its airy ward building grouped around a flowered courtyard. Its principal Hospital Loayza is similarly arranged about an open court. Increasing premedical requirements to two years of collegiate type work has helpfully reduced the freshman class from about 800 to 150 students. "Tuition" amounts to $8.00 a year. It is surprising that an 850-bed adjacent Social Security Hospital for laborers (Caja Nacional de Seguro Social, Hospital Obrero de Lima) is not utilized in teaching. Twenty eye beds are included here.

The faculty (12 in ophthalmology) under the direction of Prof. Jorge Valdeavellano is entirely part-time, and salaries are small stipends. Fourth year students in groups of 50 receive 27 didactic hours in ophthalmology, plus 27 hours in demonstration or practice techniques on each other. They do not attend any eye clinics. Interns (seventh year) spend one month on the ophthalmic service. A residency or postgraduate train-

ing program is projected but not active as yet. Elaborate theses are generally required for promotion on the faculty.

The economic balance of Peru is difficult at best, and many contrasts are seen. Huge slum areas along the Rimac river are without water or sanitary facilities and yet magnificent residential areas are rapidly expanding on the opposite side of the city. A completely new medical school plant at Arequipa has not yet been equipped or put into use.

Bogota

Colombia is currently prospering from a brief period of government stability and also the Tulane University Commission on Medical Education which has kept several workers in Colombian medical schools on long-term contracts until this year. The Old Universidad Nacional de Colombia is replacing its separated pavilion hospital with a more modern, integrated building. The 16-year-old Facultad de Medicina of the Jesuit Universidad Javeriana is developing strong concepts of good medical education under its 32-year-old Dean Bernardo Moreno. A completely new medical school is flourishing at Cali under strong Rockefeller Foundation support, and is following teaching patterns familiar to us.

Traditionally the leading school in Colombia is the National, where a freshman class of about 300 usually drops to 150 in subsequent years. There are slightly more than 100 graduates annually from the six-year curriculum. Fourth-year students receive 24 hours of ophthalmic lectures; in their fifth year, groups of 20 students are scheduled for full days of conferences, and practice examinations for 11 days. Hospital facilities are extensive and include a Cancerology Institute where ocular as well as other neoplastic diseases are grouped. The young ophthalmologist in this Institute, Dr. Gustavo Scioville S. is a dedicated man of Texan training. The 2,000-bed teaching Hospital de San Juan de Dios, has 47 beds reserved for eye. Outpatient ophthalmology is peculiarly minimized to about 15 patients each morning, who are seen by a junior faculty member in rotation. Students and residents spend very little time in out-patient clinics.

At the smaller Universidad Javeriana, tuition is quite high and classes are limited to 50. Previously inadequate hospital experience is being corrected by completion of their Hospital San Ignacio, contiguous with the medical school building. This school departs from the usual South American practice of the half-time teacher, and will have a geographic full-time faculty. Private offices for the faculty are included in the new hospital.

Summary

In summary, the current South American ophthalmic scene—as the South American cultural scene in general—presents fascinating contrasts which reflect a maturing process from the days of colonial exploitation and struggle to achieve a modern system of local education. For many generations, ophthalmic training, as many other phases of education, has remained a function of the European continent and thereby reserved considerably to the wealthy or aristocratic few. The wars and campaigns of "liberation" in the late 19th century—perpetuated in the legends of San Martin, O'Higgins, Sucre, Artigas, and Bolivar—did not produce educational or political freedom but transferred autocratic control from old family stocks east of the Atlantic to local branches west of the Atlantic. Working plans of widespread education or ophthalmic training primarily date since World War II, and in most eye centers are still in the planning stage. The brilliant ophthalmologists and other physicians, who have towered above their contemporaries, achieved some great personal contributions to medical technique but were unable to instill in their successors the concepts of fully disseminated training, fostering of subordinates, and love for investigation.

Socialization of medical practice and education similarly cannot be expected to produce over-night improvement in these pat-

terns. Political pressures and instability have also disrupted long-range training and research plans and splintered the efforts of conscientiously working physicians.

Great pride accrues in surgical finesse and clinical acumen but no centers with research orientation have developed. The heritage of earlier histologic investigators, the activity of some clinical investigators, and the growth of fine physical plants, however, give a substrata from which true eye research can evolve. Ophthalmic leaders in each university, without exception, are aware of needs in local clinical training and the beginning of at least "window ledge" investigative programs. Young ophthalmologists here and there show obvious restlessness and healthy dissatisfaction which are vital components of progress. A growing corps of young ophthalmic trainees, plus the generally obligated half-days each week to government or institutional ophthalmology, can be directed into contributing periods of critical study and first-echelon research. The resources of many huge and well-equipped government hospitals present great potential for intensive teaching programs; similarly, their huge bulk of clinical material can be correlated with investigative programs.

General educational, ophthalmic, and industrial potentials in these neighboring countries are tremendous. We must, as individual ophthalmologists and American neighbors, be attuned to intelligent participation in this sector of the world's 20th century growth.

1406 Heyburn Building (2).

THE LYMPHADENO-GLAUCOMATOUS SYNDROME*

Report of a case

Witold J. Orlowski, M.D., and Jerzy Korobowicz, M.D.
Warsaw, Poland

Lymphoid tumors are divided into five distinctive types:[2,8–10] (1) Lymphoma, (2) lymphosarcoma, (3) giant follicular lymphoblastoma, (4) Hodgkin's disease and (5) reticulosarcoma. Lymphoma is considered to represent the most differentiated type. Usually it is a circumscribed tumor of a benign character and its histologic structure approaches normal lymphoid tissue.

These views are not universally accepted. Offret[9] rejects the term, lymphoma orbitae, and accepts that of more or less malignant lymphosarcomas. He insists that, with present knowledge, one is not able to distinguish whether the tumor is malignant or inflammatory. According to him, the only way of deciding is by therapy—inflammations will respond to antibiotics and neoplasms to X-ray treatment.

Duke-Elder[2] writes that "should such a tumor occur in adult life, in either sex, if it grows slowly, does not infiltrate the surrounding tissues, shows absence of other involvement of the lymphatic system, and does not recur after removal it may be considered a lymphoma."

The percentage of the lymphoid tumors is quite considerable—10 to 15 percent. Forrest[4] among 222 orbital tumors found four lymphomas and 18 lymphosarcomas. Offret,[9] of 675 orbital tumors reported 12 as lymphoma and 99 as lymphosarcomas and reticulosarcomas. Of 251 primary orbital tumors Reese[10] found only 36 lymphoid tumors. Godtfredsen[1,6] reported eight lymphomas localized in the lacrimal gland region, among the 52 verified orbital tumors.

The ocular lymphoma may be divided clinically into three groups, depending on the location of origin and where the adenoidal

* From the Department of Ophthalmology, Military Hospital, Director: W. J. Orlowski, M.D.

tissue is present: (1) conjunctiva, (2) eyelid and (3) lacrimal gland, which is not sharply defined from the surrounding orbital tissue since the capsule of the gland is incomplete.

McGavic,[8] Heath[7] and Reese[10] showed that from one fifth to one third of these tumors are distributed fairly equally between the subconjunctival and orbital regions. The 76 cases published by Heath[7] and the 61 cases of Reese[10] presented an almost equal number of lymphoma localized in the regions: subconjunctival and palpebral (Heath, 20 percent; Reese, 30 percent) and orbital (Heath, 20 percent; Reese, 35 percent). Of Reese's cases, 15 were localized in the lacrimal glands. According to Duke-Elder[2] only a small proportion of these tumors (20 percent) are bilateral. Of the 12 cases of Godtfredsen and Lindgren,[6] seven were localized in the region of the orbit, three in the region of the orbit and palpebra and two over the eyeball in the orbit; in only four cases was the process bilateral.

Apart from the etiology of the tumor one has to consider systemic diseases—lymphadenosis aleukemia; no mention will be made of this disease in which the blood system findings explain the situation completely. Cases of this kind will have changes in the whole lymphatic system. Dzięgielewski[3] describes a case in which all the lymphatic glands of the body were enlarged.

Wittels[10] had a case in which enlarged glands were found on the neck, in the throat, at the base of the tongue, subcutaneously in the neck and in the groins. All these symptoms preceded by almost four years the eye disease. Histologically, the eye changes were described as most probably lymphosarcoma, with reticular cells present in the structure of the tumor. Dzięgielewski[3] indicated the very intensive overgrowth of the reticular cells in one of his cases.

As a fairly large number of the ocular lymphomas are localized cutaneously and subcutaneously in the eyelids, Godtfredsen and Lindgren[6] decided to compare them to the tumors occurring in the skin disease, lymphadenosis benigna cutis, described by Bäfverstedt (1943) and they came to the conclusion that lymphoma(tosis) orbitae corresponds nosologically to the lymphadenosis benigna cutis. In connection with this they considered Offret's[9] opinion as incorrect. Bäfverstedt, Lundmark, Mossberg and Stenbeck[1] published a case which denied the idea of the tumorous character of the disease—they called it lymphadenosis benigna orbitae—and considered it as a localized inflammatory process which may be found in the literature under different names: lymphoma, lymphoma simplex, inflammatory pseudotumor, and so forth.

Godtfredsen and Lindgren,[6] and Bäfverstedt, Lundmark, Mossberg and Stenbeck[1] described 13 cases and indicated the following characteristics of the disease:

The age of the patients varies from 18 to 66 years; in only four cases was the age over 50 years. Nine of the patients were women. The localization of the disease has already been mentioned. The duration of the disease is from two to three to 10 to 12 months (on an average three to four months). In one instance the disease persisted four or five years and in another 14 years. In five cases the processes were bilateral and developed more or less symmetrically and simultaneously. The tumorlike swellings grew slowly and were well circumscribed, except toward the deeper tissues, with smooth or slightly lobulated surfaces, semisolid, painless and not adherent to the skin. Two cases only had no exophthalmos. The eye movements, in some cases, were slightly restricted, though not due to ocular muscle palsy.

Ophthalmic examination, ophthalmoscopy and the visual acuity were normal and, in no case, it was emphasized, was papilledema observed. The lymphoreticular tissue, composed of the mature lymphocytes, some of them forming reactive centers of reticular and plasma cells and of eosinophil leukocytes

scattered in the tissue, was established on histologic examination. There were no epithelial cells or giant cells of the Langhans or Sternberg type.

The general state of health of the patients and especially of the hematopoietic system and of the lymphatic and salivary glands did not show any changes.

Lastly, the common feature of all the tumors is their radiosensitivity. X-ray therapy was administered in all cases, except in the first two which were submitted to operation on the suspicion of malignancy, in two or more fields to total doses of 500 to 4,500 r. The response was prompt in seven cases, in four only gradual. Recurrences of the disease were seen in two cases (under observation from one to six years) but renewed X-ray therapy gave complete freedom from symptoms. Knowing the tumor to be highly radiosensitive, Fry[5] emphasizes the fact that surgical intervention should be confined only to the biopsy in order to get a complete picture of the diagnosis.

Etiology in all the described cases was undetermined, just as in lymphadenosis benigna cutis. Bäfverstedt, Lundmark, Mossberg and Stenbeck[1] suggest that the disease process is, in some cases, a particular individual reaction to the different kinds of stimuli: inflammation, trauma, insect bites, malignant tumors localized elsewhere, and so forth.

We shall describe one of our own cases which is particularly interesting.

Case report

The patient, Mr. J. L. J., aged 76 years, an agricultural worker, lately unemployed, was admitted to the ward on July 26, 1956 (No. 4588/302/56) complaining of pain on the left side of his head and in the left eye for the last month and a half and in the right eye for four or five days. Pain in the eyes was only present when he moved his eyeballs.

On examination, the eyelids on both sides were normal. Palpebral conjunctivas were slightly hyperemic; the ocular conjunctivas had slightly dilated vessels. There were senile bands on the corneas. Nuclear sclerosis was present in both lenses. There were slightly enlarged physiologic cups on the optic discs and the spontaneous venous pulsation was visible far outside the discs on the arteriovenous crossing—Gunn's symptom.

The field of vision of the left eye was slightly narrowed (10 to 20 degrees). Vision was: R.E. 5/10, with a +1.0D. sph. = 5/6; with a +4.0D. sph. = Sn. 0.5; L.E. = 5/6.6; with a +3.0D. sph. = Sn. 0.5. Tension in the right eye was 32 mm. Hg and in the left eye, 30 mm. Hg.

All other investigations were negative. X-ray films of sinuses and orbits were negative. Blood pressure on the radial artery 180/90 mm. Hg. The intraocular pressure fluctuated during the observation period without administration of pilocarpine between 22 to 31 mm. Hg; it was slightly higher in the right eye and it rose from 22 to 34 mm. Hg in the right and to 30 mm. Hg in the left eye after the darkroom test. The intraocular pressure did not rise above 20 mm. after the administration of pilocarpine one or two times daily. Consequently the patient was discharged on August 2, 1956, but he attended as an out-patient.

He was admitted again on September 5, 1956 (No. 5334/368/56). The condition of the eye as on July 26th. Visual acuity O.U. was 5/10; with a +2.5D. sph. = Sn. 0.5. Tension, O.U., was 24 mm. Hg; blood pressure 145/80 mm. Hg.

The intraocular pressure without treatment varied during the observation period: R.E., 18 to 30 mm. Hg; L.E., 22 to 40 mm. Hg; and while on pilocarpine; R.E., 20 to 22 mm. Hg; L.E., 25 to 34 mm. Hg.

A sclerecto-iridectomy (Lagrange's operation) was performed on the left eye on September 26, 1956. Some opacity of the lens appeared after operation, which otherwise was uneventful. Intraocular pressure varied between 18 to 26 mm. Hg in the right eye and 8.0 to 16 mm. Hg in the left eye.

The patient was discharged on October 2, 1956. The field of vision of the right eye was unchanged but in the left eye the field of vision was diminished concentrically but without scotomas and without any defects.

The patient was admitted for the third time one month later on November 20, 1956 (No. 6828/472/56). He complained of headache, mainly in the left frontal region, and of exophthalmos, mainly of the right eye, and of impaired vision of the left eye.

On examination marked exophthalmos of the right eye was seen. The eyeball was slightly mobile and was surrounded by a hard ring palpable under the skin of the lids. The conjunctivas were hyperemic; the optic disc was rather shallow. The field of vision was diminished mainly on the temporal and lower sides (0 to 35 degrees). Vision was: R.E., 5/30; with a −2.5D. cyl. ax 70° = 5/6.6. Tension was 28 mm. Hg.

The left eye had a less marked exophthalmos with a hard ring, as in the right eye. The operation scar was visible. The lens was opaque but other details were not noted. Vision was: L.E.,

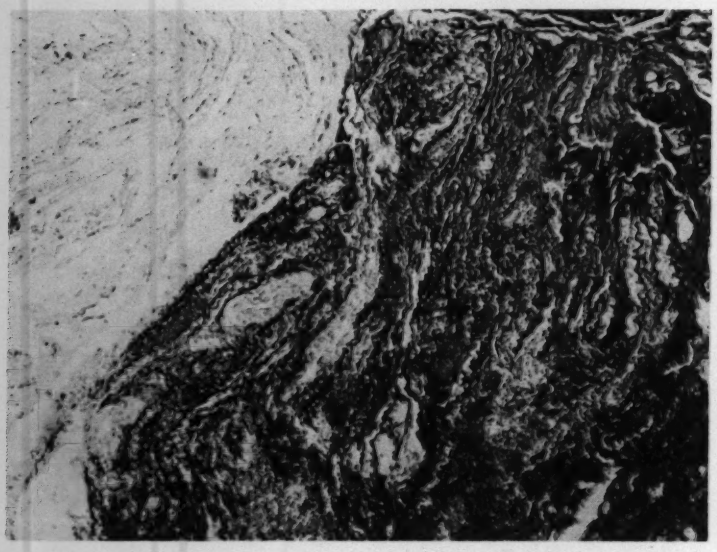


Fig. 1 (Orlowski and Korobowicz). Biopsy specimen. Reticular cells could be distinguished among the lymphocytes.

2.5/50 not improved with glasses. Tension was 24 mm. Hg. Exophthalmos was measured with the instrument resting against the bone: R.E., 29 mm.; L.E., 24 mm.

Laboratory investigations. Flocculation test, negative; Bordet-Gengou 3-9 test, negative; blood morphology, N.A.D. WBC 6.800, lymphocytes 27 percent; B.S.R., 4/11; basal metabolism, 1.0 percent; urine, N.A.D.; the binding of the complement with the rhinoscleroma was negative. Chest X-ray films showed emphysema of lungs; the sella turcica was slightly deeper than normal but the dorsum sellae was hardly visible because of decalcification; thickening of soft parts in the maxillary sinuses was present. Lymphatic nodes were not palpable.

Intraocular pressure varied between 18 to 40 mm. Hg in the right eye and 16 to 34 mm. Hg in the left eye.

A biopsy was taken from the hard ring of the right orbit on December 3, 1956. On December 17th, vision was: R.E., 5/50 + 1, L.E., counting fingers at 20 cm. The field of vision of the right eye was limited concentrically, mostly from the top 40 to 50 degrees and 20 to 25 degrees from the temporal side. Underneath the globe the ring, which surrounded the eyeball became thicker and harder in places. The patient was discharged on December 22nd at his own request.

He arrived at the hospital for the fourth time after five days (No. 7534/508/56) complaining of headache and pain in the right eye so acute that he asked to have this eye removed.

Examination of the right eye revealed marked exophthalmos (32 mm.), mobility practically nil. A hard ring of unequal thickness was palpable under the skin of the eyelid. The conjunctiva of the lower eyelid was ectropic, dry and hyperemic. The hard unindentified body which stretched the lid but did not change the appearance of the covering conjunctiva, could be palpated under the ocular conjunctiva in the upper temporal part. The anterior chamber was shallow (1.0 mm.). The fundus remained as before. Vision of the right eye was 5/50; tension, 30 mm. Hg.

The left eye showed marked exophthalmos (29 mm.) and the mobility was practically nil. The hard ring of uneven thickness was palpable under the skin of the eyelid. The conjunctiva of the lower eyelid was ectropic, dry and hyperemic. The scar of the healed fistula was seen on the limbus at the 12-o'clock position. The anterior chamber was shallow (about 1.0 mm.). The lens was opaque; the other sections were invisible. Vision of the left eye was counting fingers at 20 cm.; tension was 36 mm. Hg.

Other investigations showed 6,500 WBC, lymphocytes 31 percent. There were no changes in the lymphatic and salivary glands.

The pain and the exophthalmos increased and the ectropion became worse during the observation period. The tumor under the conjunctiva of the right eye also became larger, extending to the limbus. The intraocular pressure of the right eye varied from 22 to 32 mm. Hg and of the left eye from 32 to 38 mm. Hg despite the application of pilocarpine.

The histologic findings of the biopsy specimen showed connective, muscular and lymphoid tissue. Numerous perivascular exudates were present between the fibers. Lymphoid tissue was composed of small foci of small round cells. Some lymphocytes had accumulated among the lipoid cells and connective tissue. The bright reticular cells could be distinguished among the lymphocytes in the larger area of lymphatic tissue (fig. 1).

On the basis of the histologic and clinical examination, a diagnosis of lymphadenosis benigna orbitae, palpebrarum, epibulbar, of both eyes was made and it was decided to give X-ray therapy.

Between January 10 and February 1, 1957, the patient received 17 X-ray treatments—300 r from the lateral sides, 75 r from the anterior fields, and 100 r from the cervical regions.

The patient felt better and experienced better visual acuity even after the third treatment. Regression of the exophthalmos could be noticed after the next two treatments. The hard rings in the eyelids and tumors under the conjunctiva shrank and could not be felt any more. The exophthalmos became less pronounced and ectropion was only just visible. Headache and pain in the eyes vanished after the 11th treatment.

On February 2, 1957, the patient felt well and had no complaints. Exophthalmos and ectropion regressed. Tension was: R.E., 15 mm. Hg; L.E., 11 mm. Hg, without pilocarpine. Vision was: R.E., 5/30; L.E., hand movements. The field of vision in the right eye was reduced peripherally, but less than before, 25 to 30 degrees on the temporal side and 15 to 20 degrees inferiorly.

The patient was discharged on February 12th without any complaints. Vision was: R.E., 5/30; with a -1.5D. sph. $\bigcirc$ -1.5D. cyl. ax. 180°, $5/10 - 3$; with a $+2.0$D. sph. = Sn. 0.5.

Clinical examination on May 14, 1957, showed both eyes in normal position and no changes visible externally. A trace of infiltration could be seen in the left eye. Field of vision of the right eye was normal. Vision was: R.E., 5/10; with a -1.0D. sph., 5/5; L.E., hand movements. Tension was: R.E., 18 mm. Hg; L.E., 12 mm. Hg.

On September 12, 1957, both eyes were in normal position, the exophthalmos of both eyeballs was 20 mm. The optic disc in the right eye was very shallow. The large filtrating vesicle and a cataract were present in the left eye. Vision was: R.E., 5/15; with a -0.5D. sph., 5/5; with a $+2.0$D. sph., Sn. 0.5. Tension was R.E., 20 mm. Hg. The field of vision of the right eye was normal. Vision of the left eye was hand movements. The projection was normal. Tension of the left eye was 10 mm. Hg.

The patient died in December, 1957, from pneumonia. The postmortem examination did not reveal any metastasis or any changes in the lymphatic system.

Discussion

This case is especially interesting because of the location of the changes which occurred simultaneously in all three of the described regions and were associated with secondary glaucoma, and because of the transitory myopic astigmatism.

The presence of the lymphoidal infiltration at the base of the irises closed or narrowed the angle of filtration and so caused glaucoma which was the first symptom in our case. We assume that changes were probably too small to be proved clinically (the gonioscope alone could confirm this) but the improvement after the Lagrange operation, then occlusion of the fistula by infiltration and finally the re-establishment of the filtration and the hypotony of the eyeball after the X-ray treatment supports this view. However, we were not able to observe any hypertrophy of adenoidal tissue in the vascular membranes of the eyeball, although lymphangiomas of the uvea have been described (Miller 1906, Triebenstein 1920, Bietti 1933, quoted by Wittels[11]). Their etiology is not known. They could well be secondary lesions as, for example, in Bormacher's case (1933) also quoted from Wittels.[11]

The primary lymphatic tumor in our case occurred at the bottom of the orbit without any connection with the fornix or with the lacrimal gland. The most probable initial cause of the glaucoma were very small, invisible subconjunctival lymphoidal infiltrations around the limbus which were, however, sufficiently large to cause a disturbance in the outflow of the fluid. The theory of the independent coexistence of glaucoma and lymphadenosis benigna is less convincing; in that case it would be rather difficult to explain the regression of the symptoms of the glaucoma.

The occurrence of a complicated myopic astigmatism in an eye previously hypermetropic can be explained only by axial deformation of the eyeball, caused by the surrounding pressure. The improvement of the defect after relief of the pressure proves this explanation.

Conclusions

The problem of lymphoidal tumors is not yet solved, and there is not a single theory which would explain all the relevant problems. It may seem that, in the light of our present knowledge, it is necessary to think about malignant or benign tumors. In cases of benign tumors we have to diagnose lymphoma if the microscopic picture deviates even a little from the picture of a completely mature tissue; lymphadenosis leukemia or aleukemia (depending on the picture of blood) if the lesions of the lymphatic system are generalized; and finally, lymphadenosis benigna, if the tumors involve only one organ, if they do not show any neoplastic features and if no lesions are found in the lymphatic system. In cases of lymphoma, the lesions are most frequently unilateral; and in cases of lymphadenosis, they are more frequently bilateral. All these tumors are distinctly radiosensitive. In our case, 18 months under observation, everything points to the fact that our diagnosis—lymphadenosis benigna—was correct.

Summary

A case of proliferation of lymphoidal tissue bilaterally in the orbits, in the palpebrae and epibulbarly is described. A simultaneous glaucoma (glaucoma symptoms were the earliest), with exophthalmos and myopia (the eyes were initially hypermetropic) and without changes in the blood and in the lymphatic system, was also present. Lymphadenosis benigna was diagnosed. Under the influence of X-ray irradiations (475 r on each side in the course of three weeks) the lesions receded, glaucoma improved and the defect of refraction began to decrease. We explain the development of myopia by the circular pressure on the globe and the onset of glaucoma by subconjunctival lymphoidal infiltrations around the limbus.

ul. Polna 10/14 m. 91 (1).

References

1. Bäfverstedt, B., Lundmark, C., Mossberg, H., and Stenbeck, A.: Lymphadenosis benigna orbitae. Acta Ophth., **34**:367, 1956.
2. Duke-Elder, W. S.: Textbook of Ophthalmology. London, Kimpton, 1952, v. 5.
3. Dzięgielewski, K.: Symmetrische aleukämische Lymphadenose der Orbita. Deutsch. Ophth. Gesell. Heidelberg, 1934, Zentralbl. f. Ophth., **32**:38, 1935.
4. Forrest: Quoted by Godtfredsen and Lindgren.[6]
5. Fry, W. E.: Exophthalmos due to pathology in the orbit or adjacent structures. AMA Arch. Ophth., **56**:660, 1956.
6. Godtfredsen, E., and Lindgren, S.: Orbital, palpebral and epibulbar lymphomas: Studies on orbital tumours 4. Acta Ophth., **31**:29, 1953.
7. Heath, P.: Ocular lymphomas. Am. J. Ophth., **32**:1213, 1949.
8. McGavic, J. S.: Lymphomatoid diseases involving the eye and its adnexa. AMA Arch. Ophth., **30**: 179, 1943.
9. Offret, G.: Les tumeurs primitives de l'orbite. Paris, Masson, 1951.
10. Reese, A. B.: Tumours of the Eye. New York, Hoeber, 1951.
11. Wittels, L.: Przypadek umiarowych guzów limfatycznych zalamków spojówkowych. Przyczynek do objawów ocznych w lymphadenosis aleukaemica. Klinika Ocz., **14**:415, 1936.

BRONCHOGENIC METASTATIC CARCINOMA OF THE CHOROID*

GEMINIANO DE OCAMPO, M.D., AND ROMEO ESPIRITU, M.D.
Manila, Philippines

Choroidal metastases from a primary growth elsewhere in the body is an infrequent occurrence. In a review of the literature, Bedell[1] collected only 250 cases of choroidal metastases. A study of 4,000 enucleated eyes at the New York Eye and Ear Infirmary Pathology Laboratory by Sitchevska disclosed only 15 cases of metastatic carcinoma of the choroid, an incidence of about 0.38 percent.[2] In comparison to other eye conditions seen in the clinics, its incidence is much lower. In the Moorfields Eye Hospital of London, within a period of seven years, only two cases out of a total of 276,000 cases were metastatic carcinoma of the choroid,[3] giving an incidence of less than 0.001 percent.

Actually, however, the condition may be more frequent than statistics indicate as the condition often develops late in generalized metastases which cause death before the eye lesions can cause symptoms or are detected. Lately, more reports are creeping into the literature. Dickson[4] reports seven cases of choroidal tumors, metastatic from the breast seen at The Johns Hopkins Hospital within a period of only three years.

The most common source of the primary growth in choroidal metastases is the female breast, ranging from 65 to 70 percent of the cases.[7,8] Less frequently, in 10 to 15 percent of cases, the lung is the primary source. Other tumors which have been reported to metastasize to the intraocular structures are from the kidney, stomach, esophagus, liver, prostate, rectum, testicles, ovary and adrenals.

The following is a case of bronchogenic metastatic carcinoma of the choroid in a Filipino, probably the first to be reported in the Philippines.

CASE HISTORY

R. S., a 47-year-old Filipino, quite stocky and well built, employed in the U.S. Navy, consulted the clinic for blurring of vision and redness of the left eye. He was previously seen and treated at the Veterans Administration Hospital in Oregon for progressive blurring of vision of the left eye of three months' duration. Ocular examination revealed retinal separation, left. He was confined for one week but examinations failed to reveal the etiology of the retinal separation, although it was felt most likely to be due to a severe choroidal and retinal inflammatory process. The patient returned to the Philippines and was seen in the clinic a month later.

Examination showed a congested left eye with a dilated nonreactive pupil. The vision was negative and the tension was slightly increased (32 mm. Hg Schiøtz). Fundus examination showed a completely detached bluish gray retina (plus 20 diopters). No definite tears were appreciated and no unusual pigment disturbance was seen. Transillumination showed a dark reflex all around. The other eye was essentially normal with a vision of 20/20 — 3 J0 improved with lenses (+0.5D. sph. ⊃ +0.25D. cyl. ax. 5°) with an addition of +1.75D. sph. for near) to 20/20, J1. Tension was 15 mm. Hg (Schiøtz).

With these findings, a diagnosis of choroidal tumor was entertained. The retinal detachment could not have been merely an idiopathic one. This was based on the presence of a completely detached bluish gray retina without demonstrable tear in a glaucomatous eye and the presence of a dark reflex on transillumination. No P^{32} studies were made. With this consideration, removal of the eye was advised. The enucleation and postoperative course were uneventful. Two months later the patient started to experience backache and had coughing with blood-streaked sputum. He was referred to a lung specialist and was confined at the Quezon Institute. Three months later it was learned that he was admitted in extremis in one of the private hospitals. The autopsy revealed a tumor of the upper lobe of the right lung (adenocarcinoma, Grade II). There were pericaridial metastases with effusion which had caused cardiac embarrassment and death.

PATHOLOGIC REPORT

GROSS

The specimen consists of the whole eyeball with the following measurements: Anteroposterior, 22 mm.; horizontal, 24 mm.; ver-

* Presented at the First Scientific Meeting of the Philippine Ophthalmological Society, February 27, 1959. From the De Ocampo Eye Hospital and the University of the Philippines and the Philippines General Hospital Medical Center.

Fig. 1 (de Ocampo and Espiritu). Longitudinal section of the eyeball. There is complete retinal detachment with the subretinal space filled with a whitish albuminlike material. Note the thickened choroid at the posterior pole.

tical, 24 mm. The cornea and sclera show no abnormality. The optic nerve measures six mm. in length and 2.5 mm. in diameter.

Cut section showed a formed anterior chamber and normal lens. The retina is completely detached and with an albuminlike material occupying the subretinal space. The choroid at its posterior half is seen to be thickened and whitish in color (fig. 1).

MICROSCOPIC

The cornea appears normal histologically. At one portion of the section, the iris is soon to be adherent to the posterior surface of the cornea obliterating the iris angle, probably technical. The other portions show an open angle. The canal of Schlemm is open. The ciliary region appears normal.

The anterior lens capsule appears adherent to the pigment epithelium of the iris. The capsule is intact. There is homogeneity of the lens fibers. The vitreous cavity contains fragments of pinkish staining stringy fibrous material.

The retina is completely separated between the pigment layer and the layer of the rods and cones by a pinkish staining homogenous material containing on each side hyperchromatic cuboidal cells arranged in clumps and in acinar formation (figs. 2 and 3).

The choroid is thickened by infiltration of cuboidal and polyhedral cells producing elevation of the overlying retinal layers. The tumor cells are arranged in acinar formation and sometimes show papillary folds separated by thin bands of fibrous tissue. The cell nests show anastomosing cords, producing acinar spaces between them (fig. 4). There are foci of necrosis within those spaces composed of pyknotic cells, cellular and nuclear debris and a few inflammatory cells. The tumor cells contain moderate amounts of cytoplasm with vague syncytial bands. The nuclei are oval, rounded or irregularly nodular. There is little pleomorphism and mitotic activity.

The sclera appears normal. The optic nerve does not show any abnormality.

Examination of the histologic sections

Fig. 2 (de Ocampo and Espiritu). Section of the tumorous infiltration of the choroid and showing the detached retina.

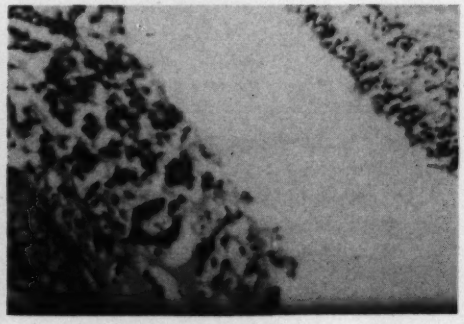


Fig. 3 (de Ocampo and Espiritu). High-power view, showing the tumor cells in the subretinal fluid. Note the acini formation.

taken from the lung tumor (figs. 5 and 6) showed the cells to have the same appearance as the tumor cells seen in the choroid. The same acinar formation is seen. By the use of special staining (mucicarmine) the tumor cells were demonstrated to be secreting mucin.

Comment

The findings on histopathologic examination of the enucleated eyeball point to a choroidal tumor with secondary retinal detachment. That was first suspected by Dr. Gloria Lim* even before the appearance of hemoptysis. That the tumor is metastatic is borne out by the following:

1. *Posterior location of the lesion.* The tumor involved the posterior portion of the eyeball. Metastatic tumors usually involve the posterior ocular structure.

2. *The acinar formation of the cells.* This denotes origin from mucosa or glandular structures.

3. *The morphology of the individual cells.* They are cuboidal and polyhedral.

4. *The ability of the tumor cells to secrete mucin.* Such a property is not possessed by any tumor cells of ocular origin.

This case is illustrative of one of those instances in which the tumor of the eye is the first manifestation of a primary tumor situated elsewhere.

*In charge of Ophthalmic Pathology, Section of Ophthalmology, Department of EENT, UP-PGH Medical Center.

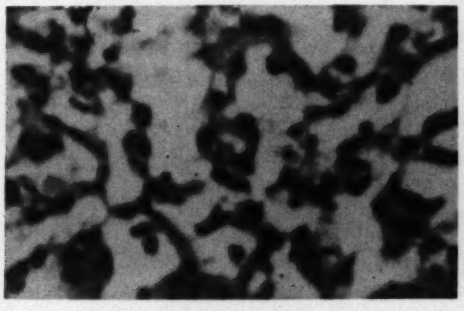


Fig. 4 (de Ocampo and Espiritu). Tumor metastases in the choroid.

Fig. 5 (de Ocampo and Espiritu). Primary bronchial site of the tumor. The cells are located at the bronchial lining. The bronchial cartilage could be seen at one portion of the slide.

Reese[5] added four of his own cases to those in the literature—one from the lung, thyroid, stomach, and the other of unknown primary site. Van Wein and Shoch[6] reported a case in which the primary growth was manifested eight months after the onset of the ocular symptoms. At this juncture, we feel it would be better if cases of lung and breast carcinoma undergo ophthalmic examination for metastases before surgery. When the tumor metastasizes from the primary site to the eye, it is usually assumed that the lungs are involved and that there must be implanted foci elsewhere.[5]

One would note that it was the left eye which was involved in this case. The involvement of the left eye is more frequent, possibly because the left carotid artery branches directly from the aorta, while the right carotid

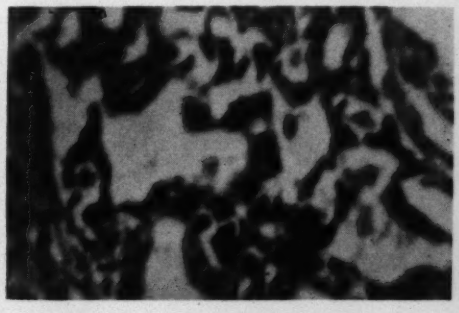


Fig. 6 (de Ocampo and Espiritu). High-power view of the lung tumor. Note the same histologic appearance as the choroidal infiltration.

comes from the innominate artery. Hence it is easier for metastatic emboli to enter the left carotid rather than the right. The majority of eye metastases usually involve the posterior pole (choroid) rather than the iris and ciliary body. Duke-Elder believes this to be due to the fact that tumor emboli have a greater chance of entering the eye through the 20 or more short posterior ciliary arteries rather than through the two long posterior or five anterior ciliary arteries.

Because of choroidal involvement, the first symptom usually is visual impairment. The retinal elevation at first would be caused by the increase in mass of the choroid involved and later to the formation of fluid which would thus simulate a serous retinal detachment. Glaucoma, which usually supervenes, could be due to any of four mechanisms:

1. Increase in size of the mass in a confined space.
2. Pushing forward of the iris-lens diaphragm, thereby producing an iris angle block. The growth of the mass is usually anterior toward the vitreous.
3. Blockage of the angle by exfoliated tumor cells.
4. Pressure on one of the large choroidal vessels, producing venous congestion.

Regarding therapy, successful treatment with irradiation has been reported by various workers. This could be employed in cases in which vision is still present. It is to be borne in mind that metastatic lesions are probably also present elsewhere and the treatment is mainly to preserve sight during the patient's remaining years and to boost his morale. In cases in which the eye is blind, congested and painful, however, enucleation would have to be done.

Summary

A rare case of metastatic carcinoma of the choroid from a primary tumor in the lung is presented. The ocular symptoms antedated those of the primary growth. The pathologic findings and physio-pathologic correlation are discussed.

932 Isaac Peral.

Acknowledgment

We wish to thank Dr. Gloria Lim for the pathologic preparation and examination of the eyeball; Dr. Augusto Camara for supplying us the clinical data about the death of the patient; Dr. Lorenzo Sunico for the autopsy report and histopathologic section of the lung and Drs. Benjamin Canlas, Amador Dimakulangan, Manuel Lim and Roberto Sunga for the photomicrographs.

References

1. Bedell, A. J.: Bilateral metastatic carcinoma of the choroid. Arch. Ophth., **30**:25-36, 1953.
2. Sitchevska, O.: Metastatic carcinoma of the choroid. Am. J. Ophth., **37**:873-879, 1954.
3. Berens, C.: Diseases of the Eye. Philadelphia, Saunders, 1950, p. 564.
4. Dickson, R.: Choroidal metastases from carcinoma of the breast. Am. J. Ophth., **46**:14918, 1958.
5. Reese, A.: Tumors of the Eye. New York, Hoeber, 1953, pp. 499-502, 505.
6. Van Wien, S., and Shoch, D.: Bilateral metastatic carcinoma to the choroid and optic nerve. Am. J. Ophth., **43**:723-730, 1957.
7. Cordes, F.: Bilateral metastatic carcinoma of the choroid with X-ray therapy to one eye. Am. J. Ophth., **27**:1355-1370, 1944.
8. Cohen, M.: Bilateral metastatic carcinoma of the choroid. Arch. Ophth., **18**:604-613, 1937.

A SURGICAL TECHNIQUE FOR CATARACT EXTRACTION BY EYE RESIDENTS*

Evaluation of cataract surgery performed by residents at Veterans Administration Hospital, Pittsburgh, Pennsylvania

Robert N. Lehman, M.D., and Murray F. McCaslin, M.D.
Pittsburgh, Pennsylvania

Introduction

In October, 1958, a diary was begun in the operating room by the chief of ophthalmology at this hospital. All pertinent details of cataract surgery performed by the eye residents were recorded. To this was added all current information of significance as these patients were followed through their postoperative stay in the hospital and the subsequent return visits after discharge.

The purpose of this was to make an active first-hand record of technique, both good and bad, as well as complications and end-results, with a view of evaluating cataract surgery done by residents. This work includes the very first eye surgery performed by three residents.

Technique

The surgical technique used was:

Preoperatively the site of operation was washed on the ward with Phisohex the night before and the morning of operation. Following this, the eye to be operated was covered with a sterile patch. Sedation is not routine but was varied according to the patient's needs. Most often it consisted of Seconal and Demerol.

At operation the skin was prepared with Phisohex and aqueous Zephiran. Mild silver protein was dropped into the eye followed by lavage of the cul-de-sacs. For anesthesia a modified van Lint injection of two-percent procaine containing hyaluronidase with adrenalin was used along with a one to two-cc. retrobulbar injection of five-percent procaine with hyaluronidase. The patient was then draped and a Guyton-Park speculum was used to separate the lids. A 4-0 silk bridle suture was placed under the superior rectus.

A wide (four mm.) limbus-based conjunctival flap was then made. With a wide flap, an extra incision of conjunctiva at the 3- and 9-o'clock positions, extending from the end of the conjunctival wound to the limbus, facilitates the handling of the flap and prevents inadvertently excising conjunctiva when completing the corneal section with scissors. A gutter was made under the flap at the limbus at the 10- and 2-o'clock positions, using a sclerotome. A 6-0 chromic gut buried suture or a 6-0 silk McLean or Mendoza suture was placed in each gutter. More sutures were introduced now or at any time later when they were indicated. Usually only two were used. If catgut was used, a suture spreader was introduced into the suture loop at the time.†

Section was then made with a keratome at the 12-o'clock position and the wound was extended with scissors to the 3- to 9-o'clock positions, the extension being eased past the preplaced sutures by the suture spreaders. A large iridectomy was performed at the 12-o'clock position.

Using the Bell erisophake, about one cc. of a 1:5000 dilution of alpha chymotrypsin was introduced under the iris at the 6-o'clock position in those cases in which this drug was used. After waiting three to five minutes the erisophake was placed onto the lens and allowed to remain there 30 seconds before any manipulations were attempted. For the beginner, the erisophake is preferred to the forceps since there is less danger of tearing the

* From the Veterans Administration Hospital and the Department of Ophthalmology, University of Pittsburgh School of Medicine.

† Lehman, R. N., and McCaslin, M. F.: A suture spreader. Am. J. Ophth., **48**:676-677 (Nov.) 1959.

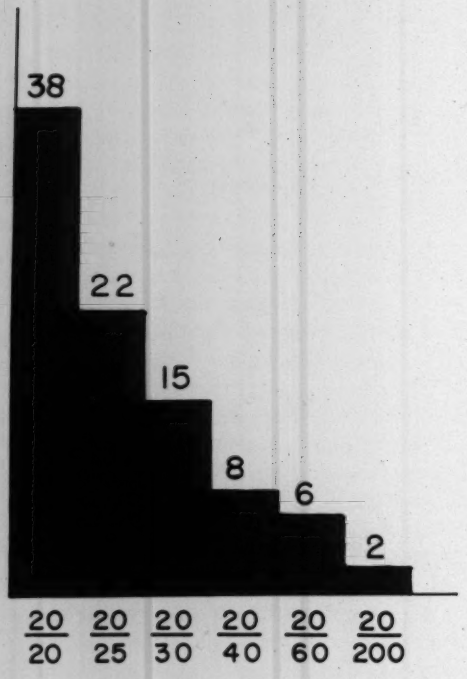


Fig. 1 (Lehman and McCaslin). Visual acuity and number of cases in which no alpha chymotrypsin was used; 82 percent had vision of 20/30 or better.

lens capsule because of inexperience. The lens was delivered by tumbling with the aid of a lens expressor. Corneal damage has not been a problem with this method of tumbling.

Introduction of alpha chymotrypsin at the 6-o'clock position usually left the zonules at the 12-o'clock position intact. This worked well with the tumbling technique and afforded some protection in the presence of liquid vitreous by maintaining a point of attachment where the lens might otherwise have sunk out of reach of the erisophake.

The wound was then closed, sutures tied, iris reposited and conjunctiva sutured. An antibiotic ointment containing a steroid was introduced into both eyes and both eyes were bandaged.

Evaluation

There were 134 eyes from which cataracts were removed surgically by residents in ophthalmology. However, seven cases were not included because, although surgery in these was successful, there were defects in the eyes at the time of surgery that prevented any chance of good vision. These defects included optic atrophy, corneal dystrophy, retinal detachment, and macular degeneration.

There were 91 cases in which alpha chymotrypsin was not used. Of these, 75, or 82 percent, had a visual acuity of 20/30 or better (fig. 1).

There were 36 cases in which alpha chymotrypsin was employed. Of these, 32, or 88 percent, had a visual acuity of 20/30 or better (fig. 2).

Figures 3 and 4 show the ages in relation to the group in which alpha chymotrypsin was not used as compared to the group in which the drug was employed. It will be seen that in the former the greater number were in the older age group, whereas in the latter the cases were distributed more nearly equally throughout all the ages.

There were nine patients under 40 years of age in which alpha chymotrypsin was employed (fig. 5). In this group 100 percent had 20/30 vision or better. In a similar group

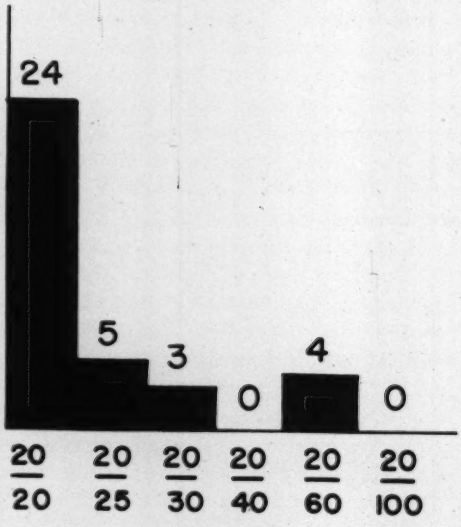


Fig. 2 (Lehman and McCaslin). Visual acuity and number of cases in which alpha chymotrypsin was used; 88 percent had vision of 20/30 or better.

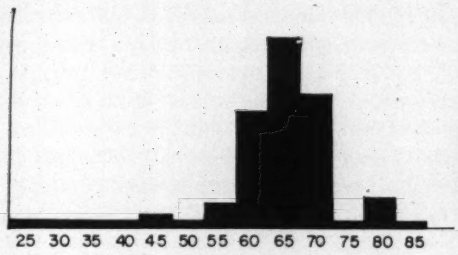


Fig. 3 (Lehman and McCaslin). Number of cases and ages in which alpha chymotrypsin was not used. Total: 91 cases.

of four in which the drug was not used 50 percent had a visual acuity of 20/30 or better. This, of course, is a small number. However, when one considers that all of this surgery has been done by residents in all stages of their surgical training, it is felt that 100-percent success in this young age group is impressive and the use of alpha chymotrypsin in patients with tougher zonules operated on by less experienced surgeons is significant.

Table 1 records in two groups faults observed during operation: cases which ended with a visual acuity of 20/40 or less and those which had 20/30 or better. Several things may be noted here. First, in spite of clumsy or faulty technique, the majority of cases do very well anyway. Secondly, in many cases, the resulting poor vision was associated with poorly placed sutures, blepharospasm during surgery due to expiration of local anesthesia, and poor delivery of the lens. Thirdly, there were no cases with poor vision associated with severe shelving of the cornea or with poor wound section, even though these defects were extreme in quite a few cases and even though these made up by far the greater number of all faults in the surgical technique.

In regard to excessive shelving and poor

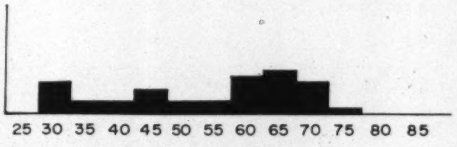


Fig. 4 (Lehman and McCaslin). Number of cases and ages in which alpha chymotrypsin was used. Total: 36 cases.

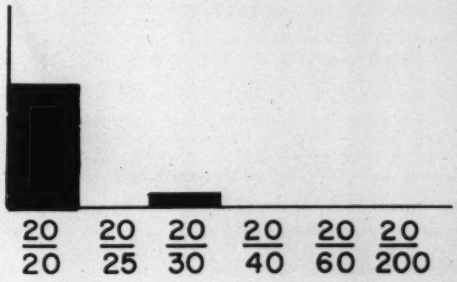


Fig. 5 (Lehman and McCaslin). Visual acuity and number of patients under 40 years of age in which alpha chymotrypsin was used; 100 percent had vision of 20/30 or better. Total: 10 cases.

sectioning, it has been said by others, and it is believed quite correctly, that, although the Graefe knife in experienced hands makes a much neater wound, this is not important if the cut edges are properly approximated. It is true that the keratome may produce an irregular or even haggled wound edge. However, if the edges are brought together so that each irregularity fits into its opposite like a jigsaw puzzle, then there is no harm and, in some instances, may even be an advantage in that a cogwheel-like mating of the surfaces may prevent subsequent slipping.

In contrast to the Graefe knife technique, it is felt that preplaced sutures should be employed when using the keratome-scissors combination to insure that any zigzags in wound edges will have the best chance for perfect approximation. On the other hand, if these zigzags are not perfectly dovetailed, then the

TABLE 1

FAULTS IN SURGICAL TECHNIQUE IN RELATION TO FINAL VISUAL ACUITY

	Vision $\frac{20}{30}+$	Vision $\frac{20}{40}-$
Sutures	9	2
Blepharospasm	1	2
Delivery	2	2
Vitreous loss	2	1
Extracapsular	4	1
Iris torn	0	1
Stitch abscess	0	1
Wound shelving	8	0
Iris prolapse	2	0
Hemorrhage, iris	1	0
Poor section	15	0

TABLE 2

RELATION BETWEEN VISUAL ACUITY ONE MONTH POSTOPERATIVE AND THREE MONTHS POSTOPERATIVE

	Cases
Visual acuity 20/30 or better which became worse after three months	1
Visual acuity of 20/40 or less which improved after three months	15
Visual acuity of 20/40 or less which became worse after three months	2
Visual acuity of 20/40 or less which remained unchanged after three months	17

keratome section is inferior to the poorest Graefe section, and most certainly will result in complications, with leaking wounds, flat chambers, iris prolapse, and astigmatism.

Since the keratome section was employed in all the cases here reported, it is for this reason that preplaced sutures were used throughout the study, two or more buried 6-0 chromic catgut (Ethicon B-790) or two or more 6-0 silk Mendoza or McLean sutures being employed. At the present time chromic catgut is preferred because it seems to produce less postoperative reaction.

Table 2 shows those cases in which there was a marked postoperative change in visual acuity. From this chart it would seem that, if vision is 20/30 or better one month after cataract surgery, the chances are excellent that vision will remain good. On the other hand, if visual acuity is 20/40 or less one month after cataract surgery, there is a 50:50 chance that vision will improve over the following several months.

Table 3 lists the complications which occurred in those cases in which alpha chymotrypsin was used. No complications occurred which could be attributed to this drug.

DISCUSSION

As mentioned earlier, this surgery is performed, under supervision, by eye residents in all stages of their surgical training. This means that many cases are the first operative procedures attempted by young surgeons. This fact presents hazards to all concerned. In eye surgery extreme delicacy is required, in addition to knowledge and skill, and failure may mean a serious life-long handicap to the patient. For these reasons it is felt that the technique taught a beginner should be as simple and easy as possible for the operator, yet safe and good for the patient. With this purpose in mind, the procedure herein described was developed at this hospital. Very little is original; everything was borrowed from others who had perfected the techniques long before they were used here. However, this operation has proved valuable in teaching residents and has been of considerable benefit to patients, as shown in the statistical report.

After the resident has attained a reasonable degree of skill in the performance of the described technique, he is encouraged to vary it, under supervision, particularly in the use of other instruments, such as capsule forceps instead of the erisophake. In this way he gradually develops a broader ability and skill with a greater feeling of confidence and less danger to the patient. The amount of variation from the basic technique will differ among residents. Those with inherent ability will develop more varied and skillful techniques, while those with lesser skill at the operating table will adhere to this basic method. It is felt this teaching affords a good foundation which insures that the resident, after finishing his training, can perform cataract surgery with reasonable chances of success.

Alpha chymotrypsin proved to be valuable in removing cataracts in 20- to 40-year-old patients. It is felt that it is particularly valuable when doctors with little surgical experience perform the operation, enhancing the

TABLE 3

VISUAL ACUITY OF LESS THAN 20/30 AND COMPLICATIONS IN CASES IN WHICH ALPHA CHYMOSTRYPSIN WAS USED

Cases	Age (yr.)	Complications
1	70	Vomited third post operative day.
2	62	No reason for poor vision
3	71	Postoperative stitch abscess with endophthalmitis during staphylococcus infection period
4	59	Retinal detachment present at time of operation

probability of good vision for the patient. This drug may also be of value when the resident is doing his first surgery in 50- and 60-year-old patients, since it produces no deleterious effect and it does make the surgery a little easier for the operator and the prognosis better for the patient. However, it is felt that alpha chymotrypsin should not be used in every case. As he progresses, the resident, as a part of his training and experience, should learn the true feel of cataract extraction without this aid.

Summary

A surgical technique for cataract extraction designed primarily for use by eye residents is described. Its relative simplicity makes it appropriate for the beginning eye surgeon. Evaluation of the results of this technique in a series of consecutive cataract cases operated by eye residents in all stages of the surgical training shows it to be reasonably safe for the patient.

Variations in this technique are discussed with a view toward gradual development of surgical skill for the resident, at the same time minimizing the danger to the patient. It is felt that, in this gradual development in skill, the resident is better trained and there is less likelihood for catastrophes or even minor surgical mistakes.

University Drive (40).

Ophthalmic Miniature

By means of Dr. von Hippel's ingenious instrument I succeeded in trephining the human cornea, through all of its layers, down to the membrane of Descemet. Seizing the edge of the circular-cut piece, I had the satisfaction of drawing it away entire, leaving a clear lining membrane to the anterior chamber of the eye. Through this clear-cut peephole vision was at once restored. Into this well from which the trephine had taken the thick plug, I inserted a disk of clear cornea cut out from a living rabbit's eye, by the same trephining instrument. The piece fitted perfectly into the hole made for it, as a bung does in the bung-hole of a barrel, its Descemet's membrane lying upon the Descemet's membrane of the human eye. The closed lid and a compress kept the graft in position.

J. J. Chisolm,
The transplanting of a rabbit's cornea into the human eye,
The Medical Record, **35**:13, 1889.

NOTES, CASES, INSTRUMENTS

COCKAYNE'S DISEASE*

A REPORT OF A CASE

WARREN J. LIEBERMAN, M.D.,
ROBERT A. SCHIMEK, M.D.,
AND
C. HARRISON SNYDER, M.D.
New Orleans, Louisiana

In 1936, Cockayne[1, 2] reported a syndrome of dwarfism associated with retinal atrophy and deafness in two siblings in an otherwise normal family of eight. Since then only five additional cases have been found recorded[3, 4] and all have been in the pediatric literature. As some of the more prominent features of this syndrome are the ocular manifestations, it would seem desirable to bring this unusual and rare disease to the attention of ophthalmologists by reporting a case encountered at Ochsner Foundation Hospital.

Cockayne's disease is characterized by a clinical onset in the second year of life of mental retardation, dwarfism with maxillary prognathism, microcephaly, large hands and feet, prominent ears, a dermatitis aggravated by exposure to sunlight, loss of fatty tissue in the face producing a somewhat senile appearance, skeletal abnormalities, carious teeth, progressive hearing loss, optic atrophy and retinal degeneration. The entire picture is relentlessly progressive with the subsequent development of intention-tremor of the hands, deafness, unsteady gait, unintelligible speech, a birdlike quickness of actions, various forms of emotional instability, and cataracts.

CLINICAL COURSE

The children are usually born without incident and seem to develop normally, or almost so, for the first year. At that time they begin to show a "butterfly type" rash on the face of a red and scaly nature closely resembling that seen in lupus erythematosis. The exacerbation of the rash on exposure to sunlight is pronounced and often is accompanied by a low-grade fever. Soon the retardation of growth becomes apparent and the lack of mental development is easily detected, in contrast to the normal members of the family. As time passes, the anatomic stigmas of the hands, feet, and head begin to appear; hearing loss is noticed; and the quick birdlike actions characteristic of the disease take the place of the more normal actions of children that age. Ophthalmologic examination at that time will disclose the ocular signs which are to be described. All of these components of the syndrome are usually fully developed by the age of five years or less.

In his 10-year follow-up report of his original two cases, Cockayne[2] described the patients at the age of 16 and 17 years, respectively, as being sexually underdeveloped, small, mentally retarded, deaf and either blind or nearly so with cataracts and optic atrophy.

OCULAR FINDINGS

Of the seven cases so far reported, a poor response to mydriasis with homatropine or Neosynephrine® was noted in four. Two of these cases had irregular pupils, and three had an abnormally high amount of hyperopia. The fundus picture in all seven was essentially the same. The retina was found to be studded with fine speckled pigment of the salt and pepper type, with the greatest concentration in the macular area. There was no apparent relationship of the pigment to the retinal vessels. The retinal venules were normal in caliber, but the arterioles were attenuated. The disc was gray to waxy with an atrophic appearance, and the macular reflex was absent. Cataracts were not present in the early cases, but seemed to develop by

* From the Departments of Ophthalmology and Pediatrics, Ochsner Clinic and Ochsner Foundation Hospital and the Department of Ophthalmology, School of Medicine, Tulane University.

the teens.[2] The following case exhibited all of these ocular signs except the pupillary abnormalities and the cataracts.

Report of case

H. A. was first admitted to Ochsner Foundation Hospital in 1957 at the age of two and one-half years with a history of recurrent butterfly-type rash, intermittent fever, and retarded physical and mental development. He was the second child born to his mother and the first to his father, and his only sibling was normal.

The pregnancy had been normal with the exception of a fall during the sixth month. Delivery was by forceps after a difficult 48-hour labor. Birth weight was seven lb. three oz. He seemed to develop normally during the first year and, except for a slight feeding problem and small stature, presented no unusual symptoms. At 15 months he began to exhibit a scaly rash over the malar and nasal regions of his face upon exposure to sunlight. Exacerbations of the rash were often accompanied by fever as high as 102°F. At this time he was able to walk, but was underweight, undersized, and did not talk. At the age of two and one-half years he was below the fifth percentile for his weight and height. The only abnormality noted on complete study of his blood chemistry, X-ray films, EKG, urinalysis and lupus cell "preps" was an elevated erythrocyte sedimentation rate. The diagnosis of lupus erythematosis was entertained, but seriously doubted. Nevertheless, he was started on steroid therapy and discharged to the clinic.

Second admission. The occasional remissions during steroid therapy were always followed by exacerbations of the rash. He was readmitted in June, 1957, some three months later, for further study. Again the entire investigation proved of no diagnostic help and it was decided to continue maintenance doses of steroids as a symptomatic treatment.

Third admission. In January, 1958 (age three and one-half years), arthritis developed in his wrists and he was admitted once more for evaluation. Results of repeat studies were again within normal limits except for a very high erythrocyte sedimentation rate, and he was discharged after symptomatic improvement of the arthritis.

Last admission. The patient was readmitted on June 23, 1960, at the age of five and one-half years with a history of continued exacerbations of the malar rash, intermittent fever, and retarded growth and mental development. At this time he was only 38.75 in. in height, weighed 28 lbs., and had a head circumference of 45 cm. According to growth charts his height and weight were those of a three-year-old and his head size was below that for the first year.

His appearance was striking. He had large prominent ears, sunken eyes, large hands and feet, prominent hips and joints, small descended testes and carious teeth. Physical examination of his chest and abdomen was negative. He was co-operative only at intervals and was quick and birdlike in his actions. He seemed to have good diurnal control of elimination, but had nocturnal enuresis for the past seven months.

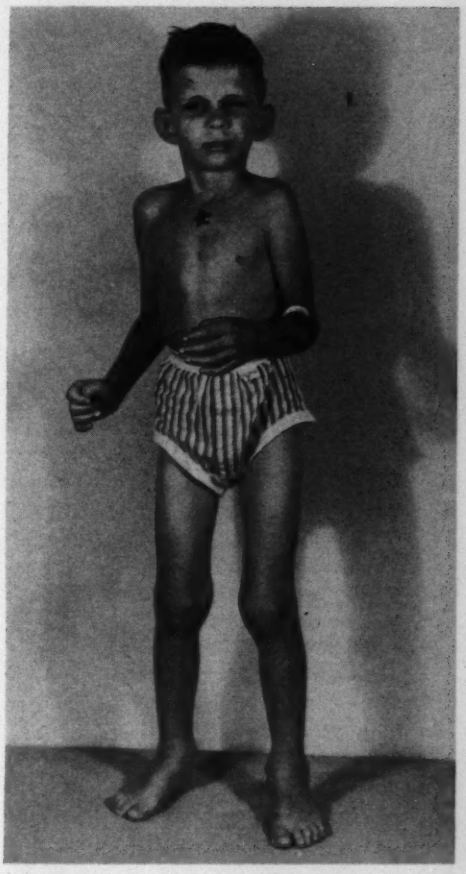


Fig. 1 (Lieberman, Schimek and Snyder). Cockayne's disease. Note the large ears, hands and feet and the enlarged knee and elbow joints.

Retinoscopy revealed six diopters of hyperopia in the right eye and three diopters in the left. Vision with best correction could only be estimated at 20/100 in each eye. The pupils were round and equal in size, reacted well to light and accommodation and dilated easily with one drop of 10-percent Neosynephrine.® The fundi presented an unusual, fine speckled pigmentation of the "salt-and-pepper" type scattered throughout the retina in no constant relationship to the vessels, but with a pronounced concentration of pigment in the macular areas. No macular reflex was seen. The retinal veins were of normal caliber to ophthalmoscopic examination, but the arterioles were attenuated to less than half the

diameter of the venules. The discs were dull and grayish. There was no nystagmus and all extraocular movements were normal. The parents stated that the child had never cried actual tears.

Results of laboratory studies on this admission were within normal limits, except for an erythrocyte sedimentation rate of 32 mm. X-ray films demonstrated a thickened calvarium, lipping of the anterior margins of the vertebrae, lengthening of the long bones of the arms and legs, and widened phalanges. EKG was again normal.

The parents knew of no such case in their families. Both parents were of English descent, but could not trace their ancestry back far enough to determine the possibility of consanguinity or relation to the cases previously reported. No ocular abnormalities were found in the parents themselves.

Discussion

The findings in the case presented here correlate well with those of the cases previously reported in the literature. The only additional feature of this patient was his seeming inability to cry actual tears. We feel that this may be added to the list of ocular manifestations previously reported as a possible part of this syndrome.

The similarity of this syndrome to progeria is readily appreciated, but there are definite differences which distiguish the two conditions as seemingly separate entities. The gross mental deficiency, retinal degeneration, disproportionate size of the hands and feet, and presence of hair serve to differentiate Cockayne's disease from progeria.[3] Investigations into the lipid status in the serum disclose only a slight abnormality of the beta lipoproteins on electrophoresis and ultracentrifugation, with entirely normal gross chemical determinations.[4] There is a suggestion of abnormal sugar tolerance, but other blood chemistry values are within normal range. Results of Toxoplasma skin test, agglutination and dye tests were normal or of no significance in two cases reported by Neill and Dingwell.[3]

At the present time, this condition is generally regarded as a hereditary abnormality.[3] There is no proved consanguinity of the parents in each of the cases reported, but all were either from England or Australia. The parents of the child reported here are both Americans of English descent, but did not know the exact locale where their ancestors lived. Thus, the question of whether this is a sporadic disease or whether all cases were descended from a single family remains unanswered at the present time. The discovery of additional cases will possibly shed more light on this most unusual and rare syndrome.

Summary

1. Seven previously reported cases of Cockayne's disease are reviewed.

2. An additional case is reported with emphasis on the ocular findings.

3. The lack of tears when crying is suggested as an additional ocular manifestation in this disease.

3503 Prytania Street (15).

Addendum

A report of this case is presently in press in the pediatric literature, with emphasis on the physical, laboratory, and chromosomal aspects of the disease.

References

1. Cockayne, E. A.: Dwarfism with retinal atrophy and deafness. Arch. Dis. Childhood, **11**:1-8 (Feb.) 1936.

2. ———: Dwarfism with retinal atrophy and deafness. Arch. Dis. Childhood, **21**:52-54 (Mar.) 1946.

3. Neill, C. A., and Dingwell, M. M.: A syndrome resembling progeria: A review of two cases. Arch. Dis. Childhood, **25**:213-221 (Sept.) 1950.

4. Macdonald, W. B., Fitch, K. D., and Lewis, I. C.: Cockayne's disease. Pediatrics, **25**:997-1007 (June) 1960.

KERATOCONUS POSTICUS*

DAVID B. KARLIN, M.D.,
AND
GEORGE N. WISE, M.D.
New York

INTRODUCTION

Abnormal variations of the anterior and posterior corneal curvatures are not common. Duke-Elder[1] divided these developmental anomalies into two groups, those with total corneal involvement and those in which only the posterior corneal surface was at fault.

Cornea plana and keratoconus have changes in both the anterior and posterior corneal curvatures and therefore belong in the first category. Keratoconus posticus, a rarer entity in the second group, is characterized by a normal anterior curvature and a loss of substance in the posterior corneal layers. It occurs as a localized lesion, keratoconus posticus circumscriptus; or diffuse as keratoconus posticus generalis. Both have a variable posterior corneal surface haze and frequent opacities.

Although the name keratoconus posticus is anatomically descriptive, it unfortunately implies a relationship to the more common conical cornea. In no reported case has keratoconus posticus progressed to conical cornea and the two are completely unrelated.

Butler[2] described the first case of keratoconus posticus in 1930. Only a few cases have been reported since. Keratoconus posticus circumscriptus is the more common type, 16 cases having been reported. Stallard,[3] Butler,[4] Goldsmith,[5] Leopold,[6] Wise,[7] Greene,[8] Guimarães,[9] and Jacobs[10] all described such cases. Keratoconus posticus generalis, the rarer form, has been reported only five times. The first case was described by Butler[2] in 1930. Ingram,[11] Ross,[12] Jacobs,[10] and De Rosa[13] have all described cases. In only one case of either variety has surgery been performed.

Fig. 1 (Karlin and Wise). Keratoconus posticus circumscriptus, O.D., viewed directly, demonstrating macular opacities with surrounding corneal haze.

The etiology of keratoconus posticus is unknown. Because of its corneal shape, Duke-Elder[14] believed this anomaly probably represented an arrest in embryonic development.

Hagedoorn and Velzebaer[15] recently described a syndrome including keratoconus posticus, lenticonus, ectopia lentis anterior and other congenital anomalies. Their case and that reported by Greene[8] have certain similar findings. In Greene's[8] case of keratoconus posticus circumscriptus, there was a macula opacity in the region occupied by the localized corneal indentation. He found anterior subcapsular cataract and a dense, round, white opacity in the fetal nucleus. Both changes were directly behind the corneal pathology. Because of the lenticular opacity in the fetal nucleus directly behind the corneal lesion, Greene[8] viewed keratoconus posticus as a congenital anomaly. He considered the corneal defect a result of delayed separation of the lens vesicle from the surface ectoderm.

* From the Department of Ophthalmology, New York University-Bellevue Medical Center.

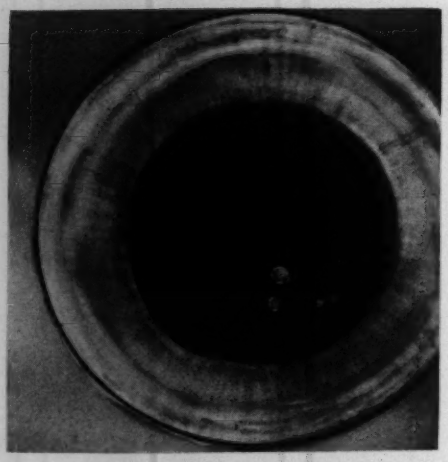


Fig. 2 (Karlin and Wise). Keratoconus posticus circumscriptus, O.S., viewed directly, demonstrating macular opacities with surrounding corneal haze.

Hagedoorn and Velzebaer's[15] 30-day-old baby had a posterior grayish indentation of the cornea. The lens fitted into this thinned indentation. The anterior surface of the lens was conical. Hagedoorn and Velzebaer concluded that this further supported delayed separation of the lens vesicle from the surface ectoderm as an etiologic factor.

Report of a case

A 74-year-old woman was first seen on August 5, 1959. The patient complained of bilateral progressive visual loss. She had no other ocular complaint and her past eye history was negative. She had definitely been able to read news print prior to her present disability. Examination revealed a corrected visual acuity of 20/200, O.D., and 20/400, O.S. Viewed directly, both corneas had macula opacities with a surrounding haze (figs. 1 and 2). In optic section, there was an increased density of the posterior corneal face in the area occupied by the corneal haze. A localized loss of substance was found here. The opacities projected back from the excavation as small rounded nubbings (figs. 3 and 4). The remainder of the corneas was completely negative. It was remarkable that such a corneal anomaly could have been compatible with adequate vision. Both eyes had nuclear cataracts with some anterior cortical lens changes. Neither fundus was visualized and the remainder of the eye examination was normal.

The decreased vision was attributed to cataracts and both lenses were extracted uneventfully. The patient had a normal postoperative course and her corrected vision was 20/40, O.D., and 20/40 + 2, O.S. She read J3, O.U. Postoperative examination of both fundi revealed mild pigment mottling and a few white spots in both maculas, which may have accounted for some of the visual loss.

Discussion

Both Greene[8] and Hagedoorn and Velzebaer[15] believed that some disturbance in the separation of the lens vesicle from the surface ectoderm was responsible for keratoconus posticus. The nubbings projecting back toward the aqueous in the present case would fit into this concept. In spite of this theory, it is still difficult to account for so much corneal pathology and the lack of lens pathology seen in this and most of the cases reported.

Figs. 3 and 4 (Karlin and Wise). (3) Keratoconus posticus circumscriptus, O.D., in optic section, demonstrating increased density of the posterior corneal face, a localized loss of substance, and opacities projecting back into the aqueous. (4) Keratoconus posticus circumscriptus, O.S., in optic section, demonstrating increased density of the posterior corneal face, a localized loss of substance, and opacities projecting back into the aqueous.

Only one report of intraocular surgery on a case of keratoconus posticus was mentioned in the literature. This was Jacob's[10] Case 4, an acute glaucoma with hypermature cataract of the right eye. An iridencleisis was performed and a postoperative infection developed, necessitating enucleation. One might think that such surgery could have a deleterious corneal effect. In our case, the corneas reacted postoperatively in a perfectly normal manner and keratoconus posticus should not be construed as a surgical contraindication.

The patient's vision following cataract extraction was 20/40 and J3. The decreased acuity was possible partly due to macular involvement. A posterior corneal defect produces little visual disturbance because the posterior corneal face is not responsible for much of the corneal refractive power. A comparable defect of the anterior corneal surface would, however, produce much visual distortion and loss of acuity because of the uneveness of the anterior refractive surface.

Linksz[16] points out that, in spite of the stronger curvature of the normal back surface of the cornea, the majority of corneal refraction is done by the anterior corneal surface. The refractive indices of the cornea and aqueous are so similar that the posterior corneal surface is relatively ineffective as an interface of refraction. For practical purposes, the cornea can be considered as a single refracting spherical interface dividing air from the inside of the eye. Therefore, the little decrease in visual acuity is predominantly due to the posterior surface haze of the keratoconus posticus rather than to its irregularity.

Summary

The findings in keratoconus posticus have been outlined and a review of the literature of this rare developmental anomaly has been made. A case of keratoconus posticus circumscriptus has been presented. It is postulated that a delayed separation of the lens vesicle from the surface ectoderm may be an etiologic factor. Furthermore, the ophthalmologist should recognize that the presence of keratoconus posticus is not a contraindication to intraocular surgery. Finally, although there are extensive posterior corneal changes in keratoconus posticus, little visual acuity is lost since the posterior corneal face is relatively ineffective as a refractive surface.

132 East 76th Street (21).
30 West 59th Street (19).

Acknowledgment

We wish to express our appreciation to Mrs. Beatrice Grover for the drawings to illustrate this case.

References

1. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1938, v. 2, p. 1280.
2. Butler, T. H.: Keratoconus posticus. Tr. Ophth. Soc. U. Kingdom, **50**:551, 1930.
3. Stallard, H. B.: Keratoconus posticus. Communication to T. H. Butler. Tr. Ophth. Soc. U. Kingdom, **50**:556, 1930.
4. Butler, T. H.: Two rare corneal conditions. Brit. J. Ophth., **16**:31, 1932.
5. Goldsmith, A. J. B.: Bilateral circumscribed posterior conical cornea. Tr. Ophth. Soc. U. Kingdom, **63**:180, 1943.
6. Leopold, I. H.: Keratoconus posticus circumscriptus. Arch. Ophth., **30**:732, 1943.
7. Wise, G. N.: Keratoconus posticus circumscriptus. Am. J. Ophth., **27**:1406, 1944.
8. Greene, P. B.: Keratoconus posticus circumscriptus: Report of a case. Arch. Ophth., **34**:432, 1945.
9. Guimarães, W.: Arch. Brasil. Oftal., **16**:209, 1953.
10. Jacobs, H. B.: Posterior conical cornea. Brit. J. Ophth., **41**:31 (Jan.) 1957.
11. Ingram, H. V.: Keratoconus posticus. Tr. Ophth. Soc. U. Kingdom, **56**:263, 1936.
12. Ross, J. V. M.: Keratoconus posticus generalis. Am. J. Ophth., **33**:801, 1950.
13. De Rosa, C.: A case of keratoconus posterior. Arch. Ottal., **63**:445 (Sept.-Oct.) 1959.
14. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, v. 2, p. 1281, 1946.
15. Hagedoorn, A., and Velzebaer, C. M. J.: Postnatal partial spontaneous correction of a severe congenital anomaly of the anterior segment of an eye. Arch. Ophth., **62**:685, 1959.
16. Linksz, A.: Physiology of the Eye: Vol. 1, Optics. New York, Grune & Stratton, 1950, p. 281.

A SMALL ELECTRIC RUST-RING REMOVER*

J. G. F. Worst, M.D.
Groningen, Holland

The small motor-driven electric drill (fig. 1) was constructed for the removal of metallic foreign bodies and their sequela, a rust ring. For this purpose it is fitted with a tiny exchangeable dental burr having spiral blades. The 1,500 rpm motor will run for three hours on a 1.5-volt hearing-aid battery.

Used as a pencil, when it is brought in contact with the corneal foreign body, a switch sets the instrument in motion and the

Fig. 1 (Worst). The rust-ring remover.

foreign body and its rust ring are rapidly worn away. Complete removal is accomplished in seconds, with the burr leaving the normal corneal tissue intact. The instrument provides a safe, accurate and rapid means of foreign-body removal.

Van Starkenborghstraat 10.

* From the University Eye Clinic (Prof. Dr. H. M. Dekking). The instrument is manufactured by the Medical Workshop, van Imhoffstraat 3, Groningen, Holland.

SURGICAL MANAGEMENT OF UNILATERAL ALMOND EYE*

Burgos T. Sayoc, Col. (MC), AFP
Quezon City, Philippine Islands

With the awakening desire of both sexes to improve physical appearance, surgeons will be confronted with cosmetic problems in the surgical management of unilateral almond eye. Similarly, the same problem will arise when the natural folds in the two lids are asymmetrical. Experience has shown that operation on the almond eye alone does not usually give satisfactory cosmetic results.

What I would like to emphasize in this paper is that, as soon as the almond eye is operated on for reconstruction of the fold, the natural fold on the lid of the other eye should be disregarded and the lid should be operated on with identical technique and measurement at the same sitting.

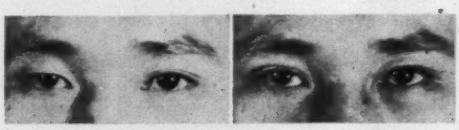


Fig. 1 (Sayoc). (Left) Before operation. (Right) Seven days after operation.

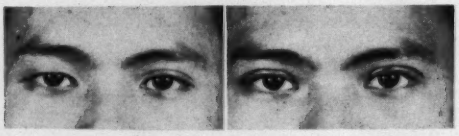


Fig. 2 (Sayoc). (Left) Before operation. (Right) Four days after operation. Sutures are still in place.

Previous to surgery, the lids are examined and an estimate of the height and size of the fold is made. Anesthesia is usually local. In as much as the construction of the superior palpebral fold had been described in previous publications,† the step-by-step surgical procedure is purposely omitted.

The results of operating both lids at the same sitting, using identical measurements and surgical techniques to produce cosmetically symmetrical folds, are shown in Figures 1 and 2.

* From the Department of Ophthalmology, Armed Forces of the Philippines.

† Sayoc, B. T.: Plastic construction of the superior palpebral fold. Am. J. Ophth., *38*:556-559 (Oct.) 1954. Westernizing oriental eyes. In Geographic Ophthalomology (W. J. Holmes), Springfield, Ill., Thomas, 1959.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

Address original papers, other scientific communications including correspondence, also books for review to *Dr. Derrick Vail, 700 North Michigan Avenue, Chicago 11, Illinois;* Society Proceedings to *Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Manuscripts should be *original copies,* typed in *double space,* with wide margins.

Exchange copies of the medical journals should be sent to *Dr. F. Herbert Haessler, 561 North 15th Street, Milwaukee 3, Wisconsin.*

Subscriptions, application for single copies, notices of changes of address, and communications with reference to advertising should be addressed to the *Manager of Subscriptions and Advertising, 664 North Michigan Avenue, Chicago 11, Illinois.* Copy of advertisements must be sent to the manager by the 10th of the month preceding its appearance.

Change of address notice should be received not later than the 10th of the month prior to the issue for which the change is to go into effect. Both old and new addresses should be given.

Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Fifty reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, George Banta Company, Inc., Curtis Reed Plaza, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

PROGNOSIS OF THE EYE SIGNS OF GRAVES' DISEASE*

A good deal is now known about the biochemistry of hyperthyroidism (though its underlying cause still eludes us), but the mysterious eye changes which often accompany it remain as enigmatic as anything in medicine. Sir Russell Brain[1] has usefully summarized what little is known about exophthalmos and the other eye signs of Graves' disease, and concluded that no single known factor can be the sole cause. Hyperthyroidism as such cannot be primarily responsible, since exophthalmos can (and often does) advance at the very time when hyperthy-

* Reprinted from *The Lancet,* June 11, 1960, p. 1286.

roidism has been brought under control by medical or surgical means. Nor can the thyroid-stimulating hormone (T.S.H.) be the only causal factor, since blood-levels of this hormone are most consistently raised in spontaneous myxedema, in which exophthalmos is never found. Yet, though neither thyroid nor pituitary hormones are likely to act in isolation, these cannot be excluded as possible factors in the production of exophthalmos.

In such an obscure condition treatment is inevitably empirical and its effects uncertain. Brain recommends that hyperthyroidism, when present, should be treated, and in severe cases he recommends tarsorrhaphy, irradiation of orbit and pituitary, and surgical decompression as necessary. He has not been impressed by the effects of hormonal treatment. No measure applied at an early stage of progressive exophthalmos can be relied on to prevent worsening of the eyes.

Although treatment is unsatisfactory, at least prognosis should be possible. This demands knowledge of the long-term history of the disease, which hitherto has not been available. Now, however, Hales and Rundle[2] have made a quantitative study of 104 patients with Graves' disease, whose eyes were carefully measured at the beginning and end of a 15-year period. Three aspects of the ocular manifestations were studied separately: exophthalmos, ophthalmoplegia, and lid retraction. In 75 patients, exophthalmometer readings were unchanged; in 24 exophthalmos had increased; and in five it had decreased by more than two mm. Thus, judged by objective measurement, the actual protrusion of the eyes usually remained unchanged, but was more likely to increase than to decrease. Ophthalmoplegia remained unchanged in about two thirds of the patients, increased in six, and decreased in four. In this respect, the score was about "all square." Spastic retraction of the upper eyelids ("lid retraction"), on the other hand, disappeared in 60 percent of those who showed this sign initially, and decreased in most of the remainder. Since lid retraction makes the eyes appear to protrude (even when they do not actually do so), and is responsible for a great deal of the ocular disfigurement in Graves' disease, its notable tendency to disappear with time led to a great improvement in the appearance of the patients' eyes. Thus in the series as a whole most patients felt that their eyes were much better, although objective measurements of exophthalmos and ophthalmoplegia showed either no change or deterioration. Hence in advising patients with the ophthalmic manifestations of Graves' disease they may justifiably be told that the appearance of the eyes will improve with time. This is a great help to their morale, which usually needs all the support the physician can give.

Discussing these findings, Hales and Rundle support Pochin's[3] suggestion that the factors responsible for initiating exophthalmos may be quite different from those which maintain it over long periods. Pochin suggested that the initial protrusion might be permitted by weakness of the extrinsic eye muscles; this would leave a space in the orbit behind the eyeball, and a neat experiment in rabbits showed that spaces in the body are commonly filled by fat. A hypothesis of this sort would account for Rundle and Pochin's[4] finding of an excess of fat in the orbit in most cases of Graves' disease, whether or not eye signs had been recognized during life.

The clinical course of the eye lesions, although unpredictable in detail, usually conforms to the same general pattern. A period of fairly rapid progression, lasting a few months, is followed by a very much longer period when the eye signs remain essentially static. There is danger to the eyes only during the initial phase of progression, and it is then that the difficult decision has to be made whether radical measures should be applied. Once the eyes have become stabilized they are no longer in danger, but may remain a source of great embarrassment to the patient. Fortunately the eyes tend to look less con-

spicuous with the passage of time, even though objective measurement shows no decrease in the actual degree of protrusion.

REFERENCES

1. Brain, R.: Lancet, **1**:109, 1959.
2. Hales, I. H., and Rundle, F. F.: Quart. J. Med., **29**:113, 1960.
3. Pochin, E. E.: Clin. Sci., **8**:97, 1949.
4. Rundle, F. F., and Pochin, E. E.: Clin. Sci., **5**:51, 1944.

OBITUARIES

CECIL HOPKINS BAGLEY
(1893-1961)

Dr. Cecil Hopkins Bagley died suddenly in his home in Baltimore on April 13, 1961. He was born in Bagley, a small community in the vicinity of Belair, Maryland, on August 17, 1893. He was the son of Charles, Sr., and Ella (McCauley) Bagley. His father was a prominent physician in Harford County and his brother, a noted brain surgeon, was for many years head of the Department of Neurosurgery at the University of Maryland.

Dr. Bagley received an A.B. degree from the Johns Hopkins University in 1917, and the degree of Doctor of Medicine from the Johns Hopkins University School of Medicine in 1921. Following his graduation from medical school, he had four years of residency training in the Department of Surgery at the Johns Hopkins Hospital. During this period of training he served under Dr. William Halstead and Dr. John M. T. Finney in general surgery. He also worked with Dr. Walter Dandy in neurosurgery and Dr. Staige Davis in plastic surgery.

In 1925 when Dr. William H. Wilmer came to the Johns Hopkins Hospital, he expressed a desire to have as his first resident someone who was thoroughly trained in general surgery. For this reason he selected Dr. Cecil Bagley, who was then a resident on the surgical house staff, to be his first resident in the Wilmer Ophthalmological Institute.

After the completion of his residency, Dr. Bagley entered the private practice of ophthalmology in Baltimore. He rapidly acquired a large following of interesting patients. During his many years of practice and teaching of ophthalmology, Dr. Bagley developed many devoted and loyal friends who appreciated his kindness and greatly mourn his sudden passing.

A. E. Maumenee.

ARTHUR M. CULLER
(1899-1960)

Arthur M. Culler was born in Mt. Morris, Illinois, December 10, 1899, the son of David and Mina Hoover Culler. In 1920 he received his A.B. from Mt. Morris College, where his father was professor of ethics. His M.D. was obtained at the University of Michigan in 1926. He interned at the University Hospital, Ann Arbor, in 1926-27 and was a resident in ophthalmology there from 1927-30. At this time he became a clinical assistant and then instructor in ophthalmology in the university, during which period he was the John E. Weeks fellow in ophthalmology and prepared his first paper on "Anatomical studies of the retina."

He then entered private practice in Dayton, Ohio, where he met and married Mary Swartsel. During this period he found time to do research work with the Kettering Foundation on the physiology of the eye, particularly on the effects of fever therapy. At this time too, he enlisted in the Dayton U. S. Naval Reserve Unit, which was among the first to be called to active service after Pearl Harbor. After a briefing period at San Diego, his hospital unit was dispatched to Efate, New Hebrides, in March, 1942, when these islands were approximately the only important group in the South Pacific not yet overrun by the Japanese. In 1944 he was transferred to Portsmouth, Virginia, as chief of ophthalmology. He retired from active service in the Navy with the rank of

ARTHUR M. CULLER, M.D.

Captain in 1946 but continued as consultant in ophthalmology to the Surgeon General, U. S. Navy, until his illness.

Following the death of Dr. Albert Frost in the fall of 1945, Dr. Culler was asked to come to The Ohio State University as professor of ophthalmology and chairman of the department, a duty which he assumed upon his retirement from the Navy. During this period he published some 20 papers, all important contributions to ophthalmolgy. Some were the result of pure research in his early years, the majority on clinical subjects encountered in private practice. His general medical services included membership on the A.M.A. Committee for Industrial Eye Efficiency, 1939-47, and chairman of the National Interprofessional Committee on Eye Care. In addition to the American Ophthalmological Society, he was also a member of the American Academy of Ophthalmology and Otolaryngology, which he served many years as an instructor in the instructional program and participated in the formal program discussions and symposia. He was also a member of the American Medical Association, the American College of Surgeons, the American Association for Research in Ophthalmology, the Columbus Medical Academy, and the Columbus Ophthalmology and Otolaryngology Society.

Ralph O. Rychener.

CORRESPONDENCE

INTRA-TENON CAPSULE INJECTION

Editor,
American Journal of Ophthalmology:

The therapy of central serous retinopathy has been most unsatisfactory and many different agents are used. These include vasodilators, barbiturates, vitamins, intravenous typhoids, and microwave therapy, to mention only a few. Due to the fact that our knowledge is so fragmentary, or really lacking as to the etiology, this is understandable.

I wish to report to you the following case in which a new therapy was used. I trust you will publish this and that other ophthalmologists will treat cases of central serous retinopathy in a similar fashion so that a series of cases can be collected for statistical analysis. The average ophthalmologist sees two or three cases a year and, from his own personal experience, he probably would not have an adequate series from which to draw a conclusion. I would be most happy if those who undertake such treatment would report to me the individual cases so treated and at a later date I would report the results to you as the editor of THE AMERICAN JOURNAL OF OPHTHALMOLOGY. In this way, it is hoped that a large enough series will be collected to prove or disprove the value of such therapy. In reporting this, I realize totally and completely that one case proves absolutely nothing and that spontaneous recovery occurs with any form of treatment, as well as with no treatment. This may be true in this one case.

On November 2, 1960, J.W.C., a white man,

aged 40 years, consulted me concerning "fuzzy" vision in the right eye which had been present for approximately three weeks. His refraction was obtained from an optometrist in January, 1960, and had been satisfactory for far vision until this episode. He noted in addition to the fuzziness that objects appeared a little dark with this eye. He was inclined to contribute his defective vision to a garden spray which he had used a few days before, since a small amount had splashed into the right eye. The left eye gave no symptoms but he realized his near vision had gradually failed in both eyes.

Vision was 20/50, R.E.; 20/20, L.E., and was correctible to 20/50, R.E.; 20/15, L.E., with his old prescription (+1.25D. sph. ⊃ +0.75D. cyl. ax. 95°) for each eye. The anterior segment by microscopy was entirely negative. The pupils were three mm., round, equal and retracted normally. The intraocular pressure was 5.5/7, equal 12.

The refraction showed: R.E., +2.5D. sph. ⊃ +0.75D. cyl. ax. 90°, 20/20 − 2H; L.E., +1.0D. sph. ⊃ +0.75D. cyl. ax. 75°, 20/15 + 4. The accommodation measured three diopters in each eye and a +1.25D. add gave J1 in each eye.

The fundus was seen clearly. The entire posterior pole of the right eye showed definite edema and there was a wide corona of light around it. The macula itself had lost its architecture, was somewhat indistinct and definitely swollen. This was confirmed by the Hruby lens on the slitlamp. The left fundus was considered normal, and remained so all during the observation. As might be anticipated, a one-mm. white target showed no central field defect.

On his original visit, he was given 0.3 cc. of a saline suspension of hydrocortisone intracapsularly in the right eye. This was again repeated on November 10th. By November 28th, he reported definite improvement in his vision, which was now 20/15-2. The edema of the macula had definitely improved and the fine details of the posterior pole and macular area were clearly discernible. On this date also, he again was given 0.3 cc. with the instructions to return in one month. He reported his vision in this eye was almost as clear and as good now as the vision in the left eye. On December 29th, the right fundus showed slight stippling in the central cecal area and immediately nasal to the macula. There were many pale punctate spots around the posterior pole, but there was no edema, no hemorrhage and no corona. The fovea was a pale spot surrounded by a red reflex. Again, he was given 0.3 cc. of hydrocortisone intracapsularly.

On January 17, 1961, the refraction of the right eye had shown a definite decrease in the hyperopia and now with a +0.75D. sph. ⊃ +0.75D. cyl. ax. 90°, vision was 20/15-1. The retina was flat. While a few pale punctate spots and slight stippling still persisted the macula was the same as in the normal left eye. The reduction in hyperopia, as well as the visual improvement, clearly indicated the absorption of the edema of the macular area.

A brief word about the method of injecting the hydrocortisone. A 26-gauge, one-inch needle is used, and the eye is turned toward the homolateral shoulder. The injection is then given in the upper inner quadrant, placing the solution as close to the optic nerve and the posterior ciliary circulatory system as possible. It is not used as a retrobulbar but as an intracapsular injection into Tenon's capsule. The needle is directed toward the macula rather than the apex of the orbit. Several drops of a local anesthetic are used and 0.3 cc. of a saline suspension of hydrocortisone acetate for soft tissue injection (each cc. of this solution equals 25 mg.) is injected.

Thanks very much for publishing this communication. It is hoped that adequate cases will be reported to warrant further investigation.

(Signed) Harold M. Block,
Dallas, Texas.

BOOK REVIEWS

DER AUGENARZT: VOLUME III. By Karl Velhagen (with the co-operation of A. Heydenreich, H. Rieger, G. Günther, H. Sautter, P. Siegert, F. A. Hamburger, and K. Hruby). Leipzig, Georg Thieme, 1960. 1,194 pages, 823 illustrations, some in color. Price: DM 194.50.

This entire volume is devoted to the morbid conditions of the eye and its adnexa, continuing the systematic presentation which commenced in Volume II with chapters on the lacrimal apparatus and the sclera (reviewed in THE JOURNAL, 49:1066 [Aug.] 1960).

Andreas Heydenreich discusses the diseases of the lids. The main divisions are: changes in the size and form of the lids and lid fissures; disturbances in the position of the lids; disturbances in the motility of the lids; inflammatory diseases of the lids; degenerative processes; color changes of the lids; diseases of the cilia; traumas to the lids; and lid tumors. Each of these divisions

has innumerable subdivisions, with an entire paragraph devoted to each entity. This form of presentation allows for easy reading for the student seeking a systematic treatment of the material, as well as for the clinician interested in a handy reference to a particular subject. There is a wealth of excellent illustrations—most of them from the author's own collections—of practically every form of disease mentioned. Therapeutic measures recommended are up to date without neglecting older and time proven procedures.

Whether by coincidence or design, Herwigh Rieger follows the same approach in his chapter on diseases of the conjunctiva. With few exceptions (for which proper credit is given) he likewise uses the beautiful illustrations of his own collection to supplement his text. In his chapter on trachoma there is no reference to the investigations of Collier and Sowa—mute evidence of the deplorable fact that even the best textbook may be dated to some extent the minute it comes off the press.

Georg Günther's chapter on diseases of the cornea is equally satisfactory from the standpoint of the clinical appearance, including slitlamp pictures, as from that of the histopathologic findings.

Hans Remky's section on the aqueous is one of the shortest in this volume. This self-effacing limitation is disappointing because Remky, next to Amsler, has made some of the most revealing contributions to our knowledge of the pathology of the vitreous. His masterly condensation of the physiopathologic, and clinical aspects is lucid enough to guarantee a clear grasp of these principles. As an example, the principle of action of the carbonic anydrase inhibitors should be cited. There is a discussion on the anterior chamber puncture (Remky himself condemns the term "puncture" for psychologic reasons, and prefers "withdrawal"). The methods determining the aqueous contents of protein factions, the cell count and differential count, the proof and identification of bacteria, and the demonstration of antibodies are beyond the resources of most laboratories available to ophthalmologists. This is perhaps the main reason why this procedure has failed to gain widespread acceptance.

Hans Sautter gives an excellent account of the pathology of the lens. His beautiful and characteristic illustrations are in effect a fairly complete "atlas" on the biomicroscopic changes of the lens. However, he does not limit his presentation to the morphology. Particularly, in his discussion of the various froms of cataracta complicata, he gives, in each instance, a minute picture of the underlying systemic disease from the etiologic, pathologic and—in some instances—therapeutic point of view. Recent investigations by Theobald and H. Gifford concerning exfoliation of the lens capsule are not mentioned. This, and perhaps the omission of a few other details, diminishes in no way the value of Sautter's really worthy contribution.

Outstanding is Peter Siegert's chapter on diseases of the orbit. His brief outline on the anatomy is not a repetition but rather a supplement to the corresponding chapter in the first volume. The wealth of material—obviously most of it observed by the author himself—is overwhelming. Since hardly any subject in ophthalmology poses so many differential diagnostic difficulties as orbital lesions, Siegert's method of approach is singularly appropriate: he illustrates practically every entity by a representative actual case report. Some of the diagnostic and therapeutic errors mentioned in these case reports are much more illuminating than a purely didactic enumeration of facts which have to be considered in the differential diagnosis.

A thoroughly up-to-date description of the motor anomalies is contributed by Franz Anton Hamburger. Some of the neurophysiologic aspects have been adequately covered by Monjé in Volume I. Here we find an outstanding discourse on the perception of space and movement. Pleoptics are discussed in great detail. In a thought-provoking anal-

ysis, Hamburger stresses that early treatment with the familiar and time-proven methods is preferable to the time-consuming, expensive, and complicated methods of pleoptics in neglected cases. There are a few important appendices at the end of this chapter. It might be wise to glance at these appendices before evaluating the main sections. Otherwise one might be surprised to find that Hamburger advises a myectomy of the inferior oblique at its origin rather than a recession of the muscle at its insertion. The latter approach is recommended in one of the appendices; here we also find some remarks on surgical procedures on the superior oblique. Likewise, the A and V syndromes are mentioned only at the end of the chapter. Incorporation of these corrections and supplements at the appropriate place in the text in a future edition will help to avoid some confusion.

The concluding chapter on diseases of the vitreous is by Karl Hruby. It is only 10 years since the same author published his book on the slitlamp microscopy of the posterior section of the eye. It is greatly due to Hruby's efforts that, during this decade, a method which formerly had been only a research tool has become everyday routine in the practice of ophthalmology. There is a brief review of the normal anatomic findings, but no technical details on the various methods of examination. In his earlier publication Hruby gave the impression that hemorrhages would not permeate into the vitreous but that "vitreous" hemorrhages actually were subvitreal hemorrhages. If this impression is correct, such a view certainly is not in accord with histopathologic findings. His present publication makes it quite obvious that hemorrhages into the vitreous actually can be demonstrated by means of posterior biomicroscopy. A very interesting observation is that a therapeutic vitreous withdrawal need not be replaced by Ringer's solution, cerebrospinal fluid, or donor vitreous. The excellent biomicroscopic illustrations are in many instances supplemented by sketches of the underlying pathologic process.

This third volume is not only ideally suited for systematic study but also as a ready reference for the practicing ophthalmologist—this in contrast to the opinion expressed in regard to the first two volumes. The print is clear throughout, the illustrations are superb, and the bibliography leaves nothing to be desired. Even if the concluding volume should not maintain the level achieved so far—and there is no reason to anticipate such a disappointment—it is obvious now that the complete work will take its place among the few outstanding textbooks in the world literature of ophthalmology.

Stefan Van Wien.

CURSILLO DE TRACOMATOLOGIA. By J. Casanovas, (with the collaboration of H. Arruga, J. Martinez-Borso, E. Mawax, A. Pumarola, and J. G. Sanchez-Lucas). Barcelona, 1960. 49 figures in black and white and 18 in color. Price: Not listed.

This monograph is based on lectures given by Casanovas and his associates in the Faculty of Medicine, Barcelona, on the various aspects of trachoma. The first chapter, by Arruga, is a historical survey with special reference to the past and present distribution of the disease. The second chapter on etiology, by Pumarola, deals with the laboratory aspects of trachoma and gives a detailed account of the recent successful cultivations of the virus and of attempts to develop a useful vaccine. In the third chapter Pumarola discusses epidemiology and provides interesting figures on the distribution of the disease in Spain, citing villages with trachoma indices varying from 24 to 80 percent. He analyzes the various factors leading to the spread of the disease.

The histopathology is discussed by Sanchez-Lucas and is well illustrated with photomicrographs. Casanovas follows in Chapters 5 through 14 with considerations on symp-

tomatology, clinical forms, complications, classification, diagnosis, prognosis, prophylaxis, and treatment. The clinical signs of the disease are beautifully illustrated by drawings and by both black and white and color photographs. The surgery of entropion and trichiasis is described fully by Mawas with diagrams and photographs illustrating all the major procedures. He also discusses fully in a following chapter the problems concerned with intraocular surgery in active and cicatricial trachoma. In the final chapter Martinez-Borso describes the antitrachoma campaign in Spain and cites figures to show a steady drop in the incidence of the disease since 1945. He makes special note of the help in this campaign given by WHO and UNICEF since 1951.

This volume provides much of interest to both ophthalmologists and public health physicians.

P. Thygeson.

A Study of the Achromatic Visual Functions in the Congenital Sensory Abnormalities of the Human Eye and in Some Amphibians and Reptiles. By Guy Verriest, M.D. Brussels, Arscia Uitgaven, 1960. 481 pages, 98 figures, 56 tables, bibliography. Paperbound. Price: Not listed.

Achromatic visual function is defined as including all properties of the eye not directly connected with chromatic discrimination, such as visual acuity, visual field, dark adaptation and the electrogram. The author's experiments on human subjects show that the photopic visual field for white is normal in protanomaly and protanopia, in deuteranomaly and deuteranopia and in the different varieties of congenital night blindness. A normal scotopic central scotoma in dark adaptation is found in protanomaly, protanopia and deuteranomaly but not in essential night blindness. Verriest confirms the findings of Walls and Mathews that Maxwell's spot is not seen in deuteranomaly and deuteranopia. In normal subjects, dichromats and anomalous trichromats, adaptation studies show three bends—the first corresponding to heterogeneity in the photopic system, the second to transition between photopic and scotopic vision, and the third to heterogeneity in the scotopic system. In essential night blindness, the curve is reduced to the photopic section and the electroretinogram shows an absence of the b-2 wave. The abnormal color of the eyeground in Oguchi's disease is due to the accumulation of a product of rhodopsin metabolism. In the electrogram of amphibians and reptiles, the latency and duration of all components of the response are greater in the nocturnal group (salamanders, toads and crocodiles) than in the diurnal group (lizards, agamids and ignanids). In the duplex retinas after light adaptation, the waves are both quicker and sharper. The relative rapidity of photopic deflections and the relative sluggishness of scotopic deflections is definitely significant.

The appendix of this important monograph from the University of Ghent contains detailed summaries in French and English. However, the Flemish text, almost identical with Dutch, is not much more difficult to read than Interlingua.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Bengisu, N. and Sezer, N. **Isolation of the Behçet virus from a hypopyon.** Bull. et mem. Soc. franç. d'opht. **72**:168-174, 1959.

The virus of Behçet has been isolated previously by Sezer at the Ophthalmological Institute at the University of Istambul. It was, at this time, obtained from the blood and the spinal fluid of patients with this disease. It was also found in the subretinal exudate of enucleated eyes but it has never before been found in the anterior chamber. Relentless efforts and extensive laboratory studies enabled the authors to prove the existence of the virus in the hypopyon of eyes with this disease. They transplanted adequate material on the chorio-allantoid membrane of the chick embryo and into the brain of mice. The difficulties in the identification of the virus are many. Its existence is temporary and fugacious and it can only be discovered by anterior chamber puncture at an early period. Individual identification of the virus in this group of diseases as well as in allied diseases like the Vogt-Kojanagi disease will be the subject of future investigations.

Alice R. Deutsch.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alagna, G. and Pandolfo, G. A. **The action of tioctico acid on the motor and sensory activity of vision.** Arch. di ottal. **64**:211-219, July-Aug., 1960.

Tioctico acid is an animal amino acid containing sulfur. The authors show an increase of central critical fusion frequency after intravenous injection of 20 milligrams of this substance. There was no effect on visual acuity, heterophoria, retinal rivalry, or fusional amplitude. (2 tables, 12 references) Paul W. Miles.

Alagna, G. and Petrosillo, O. **The effect of tranquillizing drugs on the critical fusion frequency.** Arch. di ottal. **64**:237-249, July-Aug., 1960.

The authors present an extensive review on tranquillizing drugs with many references to their effect on glaucoma; 75 patients were tested, 43 of whom had glaucoma. In 15 normal subjects, flicker

fusion frequency decreased about 20 percent after 1600 milligrams of meprobamate in 24 hours. The decrease was even greater in the peripheral retina. Librium, in a dosage of 80 milligrams in 24 hours, produced a decrease of critical fusion frequency of about 15 percent of the patients. (3 tables, 38 references)

Paul W. Miles.

Bon, W. F. and Nobel, P. C. **The Influence of immunization against eye lens protein on the electrophoretic picture of blood plasma and eye lens proteins. Preliminary communication.** Ophthalmologica **140**: 333-334, Nov., 1960.

Rabbits systemically immunized against bovine lenticular alpha-crystallin demonstrated a moderate loss of alpha-crystallin and even greater loss of gamma-globulin from the peripheral lens cortex, as demonstrated by agar electrophoresis. When stirred in a buffer solution, it was observed that the peripheral lens cortex of the immunized rabbit disintegrated and passed into suspension much more readily than did that of the normal rabbit. The only mention in the article of the plasma change (mentioned in the title) is the following: "It seems that a band occurs in the diagram on the place of alpha-crystallin, clearly outlined against the neighboring albumin band." The significance of these observations is briefly discussed. (1 figure, 3 references) L. T. Post, Jr.

Daily, Louis and Tuttle, W. S. **Experimental use of enzymes for hyphemas and conjunctival hematomas.** A.M.A. Arch. Ophth. **65**:410-414, March, 1961.

Streptokinase-streptodornase and trypsin had no observable effect on these conditions in rabbits. (3 figures, 12 references) Edward U. Murphy.

Doczy, L. **Comparative studies of the action of atropine and scopolamine in cycloplegia.** Klin. Monatsbl. f. Augenh. **138**:398-401, 1961.

The results obtained from 1,500 eyes revealed that a single dose of a 2-percent scopolamine solution equals the cycloplegic effect of a 1-percent atropine solution administered once daily over three days. (6 references)

Gunter K. von Noorden.

François, J. and De Rouck, A. **The electroretinographic response of normal subjects to coupled stimulations.** Ophthalmologica **140**:353-368, Dec., 1960.

This is yet another in a series of recent articles establishing the normal pattern of ERG responses to coupled light stimuli. Special attention is paid to refractive periods and recuperation times. The interval between stimuli is varied and the effect on the electroretinogram is noted. Variations caused by pretreatment with anesthetics, by dark adaptation, and by ether anesthesia are reported. Finally, patients with "peripheral tapetoretinal degeneration" are studied. Details of these different curves are the substance of this communication, and they are too varied to summarize. Those particularly interested should read the original article. (16 figures, 2 tables, 7 references)

L. T. Post, Jr.

Medgyaszay, A. **Transitory changes of refraction under the influence of Fonurit.** Klin. Monatsbl. f. Augenh. **138**:255-258, 1961.

Fonurit is the Hungarian equivalent of diamox. Measurements of visual acuity for near and distance, refraction, accommodation, and a slitlamp examination were made in 20 patients who were taking diamox. Transitory change of refraction was observed in one patient, and a transitory decrease of accommodative range in another. (18 references)

Gunter K. von Noorden.

Orbán, T. **Experiences with Panthesin-Hydergin (PH 203) and Exacthin (ACTH) in disturbances of retinal circulation.** Ophthalmologica **140**:388-400, Dec., 1960.

The authors are distressed by what they conclude to be an increasing incidence of vascular and circulatory diseases, and by the complications and poor results obtained by the use of anticoagulants for the treatment of these conditions. In an effort to find a less hazardous, simpler, and more effective therapy, they have treated 40 patients exhibiting various retinal vascular diseases with a combination of Panthesin-Hydergin and ACTH. Panthesin is the trade name for the N-diethylleucinol ester of para-aminobenzoic acid; it is most commonly used for surface and infiltration anesthesia. Hydergin is the trade name for a mixture of the methanesulfonates of dihydro-ergocornine, -crystine, and -cryptine; these are all adrenergic blocking agents, and consequently peripheral vasodilators; they are administered either intravenously or intramuscularly. In this article the dosages are recorded in numbers of ampoules, and hence are meaningless to those not acquainted with these specific commercial products. The rationale for their use in vascular disease is that the Panthesin, being a pananesthetic, reduces arterial spasm through decreasing the hypersensitivity of the nerve endings of the vessel walls; that the Hydergin widens the arterioles and precapillaries and reduces reflex vascular constriction, allowing for better oxygenation and nutrition of the tissues; and that the corticotropic hormone cuts down vascular permeability and its harmful consequences; namely, edema, protein exudation, and hemorrhage. Ten cases of arterial embolization and five cases of "tapetoretinal degeneration" were unimproved. "Strikingly good results" were obtained in 16 branch and 15 central vein "thromboses," and five disciform degenerations of the macula. The improvement was usually noted within three to five days, and almost invariably the maximum improvement was seen within 10 days. The improvement persisted in most instances, despite cessation of therapy. Favorable results were noted even in the face of a long history of disease, e.g., a four-year-old vein occlusion showed definite, if slight, improvement. Although the drugs were intially administered intravenously, it was later found that they were equally effective when given intramuscularly and thus could be used on an out-patient basis. The writers stress the lack of complications; prothrombin time is not significantly lowered, nor are any other laboratory findings seemingly affected. Careful observations and control are, therefore, made unnecessary. (2 tables, 25 references) L. T. Post, Jr.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

van Beuningen, E. **A new stereoscopic test chart.** Klin. Monatsbl. f. Augenh. **138**: 339-344, 1961.

A new stereoscopic test is described which is based on the principle of the angle of parallax. Guesses are reduced to a minimum or even eliminated. Results obtained with this method in 35 adult patients are reported. (1 table, 2 figures, 2 references) Gunter K. von Noorden.

Gramberg-Danielsen, B. **Dark adaptation, illumination and glare in road traffic.** Klin. Monatsbl. f. Augenh. **138**:403-409, 1961.

The significance of dark adaptation during driving, its disturbances resulting from bright illumination, sun exposure during the day, or hypoxemia in high altitudes are discussed. The driver must avoid

looking into the headlights of oncoming cars. Problems connected with glare in road traffic are mentioned. (7 references)

Gunter K. von Noorden.

Gramberg-Danielsen, B. **Problems of visual acuity and monocularity in road traffic.** Klin. Monatsbl. f. Augenh. **138**: 261-264, 1961.

The factors which influence visual acuity while driving a car are enumerated. Night myopia may affect a hyperope who is required to wear glasses, but sees much better at night without them. On the other hand, myopia may increase at night and the corrective lens worn by a myope may no longer be sufficient. Other factors disturbing vision are haze, contrast, adaptation, and glare. The special problems arising from monocularity are field loss, decreased light sensitivity in the dark, increased sensitivity to glare, and loss of stereoscopic vision. (8 references)

Gunter K. von Noorden.

Kadlecová, V. **The pupillomotorial adaptation of the eye.** Ophthalmologica **140**:379-387, Dec., 1960.

As the eye adapts to darkness the retina becomes gradually and progressively more sensitive to light. This is true also of the pupillary response. Pupillary movements can be observed in the dark by the use of infra-red light, the anterior segment of the eye being viewed through a special fluorescent screen suitably magnified. The former is a subjective test, the latter an objective one. If the dark adaptation curve of one corresponded to that of the other, observation of the pupil would provide a far superior and more accurate way of measuring this retinal function. The aim of the experiments reported in this paper was to test these two functions simultaneously and compare them. Unfortunately, the two curves were *not* parallel in the majority of instances. The authors go on to describe four varieties of "pupillomotorial" dark adaptation curves and these are briefly discussed. (5 figures, 9 references)

L. T. Post, Jr.

Meisner, R. **Treatment of amblyopia with the film visuscope after Professor Heinz.** Klin. Monatsbl. f. Augenh. **138**: 327-331, 1961.

The instrument which has been described in detail by Heinz (Klin. Monatsbl. f. Augenh. 138:315-327, 1961) was used in 24 children with eccentric fixation. Foveal fixation was achieved in seven, temporary foveal fixation in six children but visual acuity could not be influenced to better than 5/15. (2 figures, 4 references)

Gunter K. von Noorden.

Stofft, P. **Utilization of intermittent light stimuli to evaluate the development of visual function in infants.** Ann. d'ocul. **194**:133-152, Feb., 1961.

In the course of examining the electroencephalograms of infants the author investigated the response to intermittent light stimulation (I.L.S.) He finds that during the first year of life there is no cortical response to intermittent light stimulation during normal sleep. An on-off response to I.L.S. does appear in the first few months of life. At about the fifth month "driving" begins to appear and is almost constant at the age of seven months. The author feels that this finding is important in children between the ages of five and eight months where an ordinary evaluation of visual function is impossible. Furthermore, in older children with mental retardation which makes ordinary visual examinations impossible, the "driving" response to I.L.S. may indicate the presence of normal vision. This would be of particular importance in cases of delayed myelinization of the optic tracts.

In many cases one may also obtain a frontal response to I.L.S. in addition to

an occipital response. It is theoretically possible to obtain a tracing which shows a response from the frontal area and a lack of response in the occipital area. The author states that this would allow one to postulate a lesion in the geniculocalcarine neuron. (8 figures, 68 references)
David Shoch.

Ten Doesschate, G. **Vision in an empty visual field.** Ophthalmologica **140**:322-332, Nov., 1960.

The author presents a summary for the ophthalmological literature of a series of experiments published in Aeromedica, Vol. VI, 1958, pp. 9-68. It had been previously stated that pilots flying at high altitudes, and, therefore, in an empty visual field, accommodated slightly. Emmetropes would thus become artificially nearsighted and less able to recognize distant, barely discernible objects. This is a matter of some concern, considering the speeds of high altitude aircraft. It was concluded that hyperopes would be more suitable as pilots. To test this claim, a series of experiments was set up, too complex for brief summarizing. It was confirmed that young people in an empty visual field accommodate 0.25 to 1.75 diopters, and that the degree of accommodation is not influenced by the extent of the visual field, the illumination, or a simulated cockpit window frame and lighted dash-board. (These observations might also be helpful in understanding the never happily explained "night myopia.") (4 figures, 2 graphs) L. T. Post, Jr.

Welsh, R. C. **Corneal contact lens trial sets for postoperative cataract patients.** A.M.A. Arch. Ophth. **65**:427-432, March, 1961.

With the aid of corneal contact lens trial sets, the general ophthalmologist may very easily learn to fit these lenses to his postoperative cataract patients. Aphakics like them and tolerate them well. The author discusses in detail the curvatures, diameters, and powers he has found useful. (1 figure, 1 table, 7 references) Edward U. Murphy.

5
DIAGNOSIS AND THERAPY

Baum, Gilbert, and Greenwood, Ivan. **A critique of time-amplitude ultrasonography.** A.M.A. Arch. Ophth. **65**:353-365, March, 1961.

In this paper the authors call attention to the necessity of using proper techniques and instrumentation so that the full value of this diagnostic tool may be realized. They challenge some recently published reports which advocate modifications. (9 figures, 11 references)
Edward U. Murphy.

Bleeker, G. M. **Evaluation of three methods of recording the depth of the anterior chamber of the eye.** A.M.A. Arch. Ophth. **65**:369-374, March, 1961.

Serial photographic recording is more reliable than measurements with Lobeck's ocular, and both are superior to Jaeger's instrument. In the latter two instruments the observer's judgment plays an important role. (10 figures, 5 references)
Edward U. Murphy.

Brown, D. S. **The use of corticosteroids in herpes zoster ophthalmicus.** Med. J. Aust. **1**:290-291, 1961.

Four cases are presented in each of which the eye responded rapidly to dexamethasone. Pain was relieved in one or two days and post-herpetic neuralgia did not occur. Ronald Lowe.

Chodos, J. B. and Habegger-Chodos, H. E. **The treatment of ocular toxoplasmois with spiramycin.** A.M.A. Arch. Ophth. **65**:401-409, March, 1951.

Sixty-seven patients were observed for one year. The authors conclude that this

antibiotic is the therapy of choice in a single daily dose of 2 gm. combined with the judicious use of steroids. Ninety percent of the cases were considered cured. Side effects of this drug were minimal in contradistinction to those with Daraprim and sulfonamide. (2 figures. 3 tables, 65 references) Edward U. Murphy

Cristini, G. and Fiorenzi, G. **Uveal biohemo-photometry. A new method to measure uveal blood circulation in vivo.** Klin. Monatsbl. f. Augenh. **138**:216-226, 1961.

The apparatus consists of a light source for white light, filter, photoelectric cell, and an amplification system (biohemo-photometer), connected with a slit-lamp. Transscleral illumination illuminates the enlarged pupil. The color of the light transmitted through the pupil depends on the amount of blood present in the uveal tissue. Calculations essential for calibration of the apparatus are described. This procedure permits studies of the normal and abnormal uveal blood circulation, and can be successfully employed for physiological and pharmacological research. (7 figures, 1 reference)

Gunter K. von Noorden.

Crompton, D. O. **Some factors in the prevention of sepsis in ophthalmic surgery.** Med. J. Aust. **1**:356-362, 1961.

In a series of 1,321 lens extractions performed by 23 ophthalmologists at an Adelaide hospital from 1949 to 1960, nine cases of panophthalmitis led to eight evisceration and one enucleation. Factors predisposing to ocular sepsis are tabulated and more extensive consideration is given to some of them; namely, to defects in aseptic technique, infected sterilising solutions, infected scrubbing brushes, sterilisation of dressings, caps and masks, scrubbing-up, operative technique, and post-operative dressing. Infected eye drops receive special mention. Disasters from and the prevalence of contamination of eye drops are presented with methods of correcting these faults.

The author frankly describes unsatisfactory conditions that have led to loss of eyes and vision and offers lessons from which few ophthalmic surgeons could not profit. (4 tables, 18 references)

Ronald Lowe.

Dorello, U. and Palmieri, L. **The rheuma test in ophthalmology.** Arch. di ottal. **64**:261-265. July-Aug., 1960.

A serum agglutination test which is positive in rheumatoid arthritis proved to be negative in uveitis. (8 references)

Paul W. Miles.

Krishna, Narenda, Mann, M. J. and Leopold, I. H. **Manometric determination of monoamine oxidase in ocular tissues.** A.M.A. Arch. Ophth. **65**:338-344, March, 1961.

The authors report the results of their investigations concerning the activity of this enzyme in the various components of the rabbit eye. (2 figures, 6 tables, 8 references) Edward U. Murphy.

Matthäus, W. **Thermoelectric measurements in the human eye.** Klin. Monatsbl. f. Augenh. **138**:227-235, 1961.

A historical review of medical thermometry is presented. Theory and methods of thermoelectric measuring procedures are discussed. Surface measurements of cornea and conjunctiva were performed in 200 human eyes. Conjunctival temperatures were approximately 1.05° C. higher than those obtained from the corneal surface. Measurements in patients who underwent fever therapy revealed that the temperature increase of the eye follows the increase of body temperature with a latency of one to two hours. The same latency was observed, when the body temperature returned to normal. The measurements were per-

formed with a thermoelement. (7 figures, 20 references)

Gunter K. von Noorden.

Schreck, E. **Practical significance of eye manifestations in skin diseases.** Klin. Monatsbl. f. Augenh. **138**:161-175, 1961.

Diagnosis and modern therapy of the eye manifestations of the following skin diseases are briefly discussed and illustrated by case material: scrofulosis, rosacea, erythema multiforme, episcleritis, drug allergy, Behçet's, Harada's, and Vogt-Koyanagi's syndromes, psoriasis, collagen diseases, the syndromes of Reiter and Sjøgren, pemphigus, scleroderma, ichthyosis, and atopic dermatitis. Some of the rarer forms of oculodermatologic syndromes are discussed. (15 figures)

Gunter K. von Noorden.

Schubert, E. **Preliminary report on the results of ophthalmologic examination in 29 patients with ornithosis.** Klin. Monatsbl. f. Augenh. **138**:394-397, 1961.

Virological characteristics of ornithosis are discussed. The disease not only is contracted from parakeets but can also be transmitted to humans from chickens, doves, ducks and geese. Lenticular and vitreous opacities were found in 25 out of 29 patients with ornithosis. All patients had a positive compliment fixation test. The disease had occurred endemically in the area where the author practices. (1 table, 13 references)

Gunter K. von Noorden.

Slezak, H. **Privine (Ciba) as an addition to retrobulbar anesthesia.** Klin. Monatsbl. f. Augenh. **138**:401-403, 1961.

Undesired side reactions of adrenalin or its derivates called for a substitute to be added to the retrobulbar anesthetic. Privine, which has a vasoconstrictor effect, was successfully used in connection with novocaine for retrobulbar anesthesia. The ocular tension was lowered sufficiently by this procedure to perform intraocular surgery. (8 references)

Gunter K. von Noorden.

Weekers, R., Watillon, M. and Lavergne, G. **Corepraxia by photocoagulation.** Arch. d'opht. **20**:581-587, Sept., 1960.

The authors employed the photocoagulator of Meyer-Schwickerath to create clear central pupils in 41 eyes with occlusion or displacement of the pupils following 1. cataract extraction, or 2. ocular trauma with corneal perforation. They found the procedure to be well tolerated even in fragile eyes that would not have supported surgical intervention. Four of the cases are reported in detail with records of refraction and visual acuity before and after photocoagulation. A color plate with before-and-after-treatment photographs illustrates well the successes obtained. The authors suggest that the favorable results justify a search for blind patients who might possibly benefit from the procedure. (4 figures, 1 reference)

P. Thygeson.

6

OCULAR MOTILITY

Bangerter, A. **The significance of motor orthoptics with special regard to the muscle trainer and the convergence trainer.** Klin. Monatsbl. f. Augenh. **138**:305-315, 1961.

Orthoptic exercises for improvement of ocular motility are indicated as an isolated treatment for slight disturbances of the muscle balance, for muscular insufficiencies, and for muscular palsies or paralyses. In addition, these exercises are recommended prior to and after surgery for comitant and noncomitant strabismus. The muscle trainer consists of a fixation object mounted on the end of an arm which swings back and forth before the eyes and is driven by an electromotor. The head of the patient is im-

mobilized in a head rest during this procedure. The indications for the training of convergence are discussed and the convergence trainer, composed of a rotating spiral, is described. (37 figures)

Gunter K. von Noorden.

Duncalf, Deryck, and Jampel, R. S. **The acion of d-tubocurarine on the extraocular muscles in strabismus.** A.M.A. Arch. Ophth. 65:366-368, March, 1961.

The eyes of 26 patients were studied on the operating table prior to general anesthesia and it was noted that the eye muscles undergo a distinct pattern of progressive paresis after the intravenous injection of d-tubocurarine in divided doses. This general pattern was found: ptosis, paralysis of upward gaze and convergence, and paralysis of lateral and downward gaze. (1 table, 7 references)

Edward U. Murphy.

Fox, S. A. **Postoperative complications of levator surgery.** A.M.A. Arch. Ophth. 65:345-352, March, 1961.

The more common complications are over- and undercorrection, lagophthalmos, entropion, disturbances of the lid fold and lid margin, lid lag, and postoperative keratitis. The author discusses these complications and analyses their causes. (8 figures, 3 references)

Edward U. Murphy.

Heinz, K. **Film visuscope, an apparatus for the therapy of strabismic amblyopia.** Klin. Monatsbl. f. Augenh. 138:315-327, 1961.

The instrument consists of a small electrically driven microprojector which is connected with a visuscope head. Moving pictures can thus be projected onto the macula of the patient under direct control of the observer's eye. This is supposed to train the macula of the amblyopic eye with non-foveal fixation by "optic massage." Several short films have been developed in order to vary the treatment and to arouse the interest of the child to be treated. Three cases are reported where good results were achieved with this form of therapy.

Gunter K. von Noorden.

Wiesenack, W. **Comparative studies on several methods for phoria determination and their significance for prismatic correction.** Klin. Monatsbl. f. Augenh. 138: 331-339, 1961.

Phoria was determined according to the Rodavist test (Schober), the Polatest (Busch, Berlin), and the Maddox rod test in 62 patients. While the two former tests yielded similar results, those obtained with the Maddox rod differed. In order to calculate the prismatic correction in phorias, the fusional range has to be determined. A formula developed by Sheard for this purpose is discussed. (32 references.

Gunter K. von Noorden.

7

CONJUNCTIVA, CORNEA, SCLERA

Collier, M. **Frequency in France of limbal degeneration (white limbus girdle of Vogt) as a function of age and sex. Respective frequency of types I and II and of their localizations.** Arch. d'opht. 20: 588-601, Sept., 1960.

The author notes that only two authors, Goar in the United States and Marty in Switzerland, describe the frequency of the white limbus girdle of Vogt. He then reports the first French study of the condition in which he found the frequency to be 3.4 percent. Women were affected 3.7 times more often than men. No cases were found at ages below 30 years. In females the greatest frequency of the lesion was in the age group from 81 to 90 years; in males it was in the group from 51 to 60 years. Collier found type I more frequent than type II (the scleral type), with nasal localization more frequent than temporal localization in both types. In 102 subjects

with the condition, 17 percent had both types and 83 percent had only one type in the two eyes. (12 tables, 4 figures)

P. Thygeson.

D'Ombrain, A. **Deep corneal wound from Lambertia formosa (Mountain Devil).** Med. J. Aust. 1:189, 1961.

An Australian flowering tree is described which has bright red flower clusters surrounded by a palisade of yellow-green bracts, each of which ends in a needle-like spine. A case of injury is reported in which one of the spines penetrated the cornea.

Ronald Lowe.

Fechner, P. U. and Fechner, Ina. **Influence of pyrogen on healing of corneal ulcers.** A.M.A. Arch. Ophth. **65**:392-400, March, 1961.

Experiments on guinea pigs indicate that this substance intensifies reparative processes in the cornea and can exert a beneficial effect in corneal disease. (6 figures, 2 tables, 44 references)

Edward U. Murphy.

Guennec, J. and Robineau, G. M. **Note on three cases of conjunctival myiasis.** Arch. d'opht. **20**:616-619, Sept., 1960.

The authors report three cases of myiasis seen since 1958 in the region of Vence. All the patients had similar symptoms of an irritative conjunctivitis with pain, foreign-body sensation, tearing, and redness. The most prominent symptom was the sensation of moving foreign bodies. On examination the larvae were found in numbers from six to twelve, accumulated in the lower fornices. Healing of the conjunctivitis occurred rapidly on removal of the parasites. Identification of the larvae was made in only one case; they proved to be larvae of Rhinoestrus purpureus. The identifying characteristics of the larvae are illustrated in two photographs. The authors conclude with a review of the subject and note that Rhinoestrus is only a rare cause of ocular myiasis but that the first cases were found as early as 1845 in Italy by Galvagni. They mention the gravity of myiasis due to Hypoderma bovis in which the larvae can penetrate the globe. A review of recent literature is given. (2 figures, 15 references)

P. Thygeson.

Hermann, P., Hervouet and Lenoir. **A new case of corneal aspergillosis. Anatomo-pathologic appearance.** Arch. d'opht. **20**:804-809, Dec., 1960.

The authors report a case of slowly developing post-traumatic ulcer in a man 63 years of age, which had failed to respond to streptomycin and penicillin by injection and to the local use of pencillin, sulfonamides, terramycin, hydrocortisone, and methylene blue. When its fungal etiology was recognized the ulcer was 8 mm. in diameter. It failed to respond to tincture of iodine locally, to mycostatin by mouth, and later to potassium iodide by mouth and gentian violet topically. Enucleation was performed when a descemetocele and total hypopion developed. Pathologic examination showed extensive invasion of the cornea with aspergillus filaments. The article is illustrated with six photomicrographs in black and white. The authors review the reasons for therapeutic failure in this case. (6 figures)

P. Thygeson.

Hilgers, J. H. Ch. **Prevention of recurrent pterygium by beta radiation.** Ophthalmologica **140**:369-379, Dec., 1960.

"Encouraging results" were obtained in 24 eyes treated with beta irradiation (strontium-90 applicator) after various surgical procedures for pterygium. All eyes were followed at least five months. There were two recurrences. Follow-ups were admittedly not long enough to be sure that the lenses had not been damaged. (2 tables, 38 references)

L. T. Post, Jr,

van Laer, P. and Pilleri, G. **Morphological studies on the "protuberantia scleralis."** Arch. f. Ophth. **163**:1-9, 1961.

About a century ago the embryological development of a posterior scleral proturberance had been described, and has sometimes been incriminated as an etiologic factor in myopic posterior staphyloma. The authors examined and measured 94 bulbi of normal embryos at different stages of development and could not verify its existence. (5 figures, 9 references)

Harri H. Markiewitz.

Lo Cascio, G., Jr. **Biomicroscopic relief in the cornea in some cases of argyrosis of the conjunctiva.** Arch. di ottal. **64**:229-236, July-Aug., 1960.

Marmorization of Descemet's membrane is illustrated. (4 figures, 6 references)

Paul W. Miles.

McPherson, S. D. and Grace, E. V. **Catgut sutures in corneal surgery.** South. M. J. **54**:165-168, Feb., 1961.

The authors report their results with the use of 6-0 plain and chromic catgut sutures in the closure of 23 lamellar and penetrating keratoplasties and 47 corneal lacerations. Gut sutures do not require removal. This is a distinct advantage, especially in children. There seems to be no more corneal scarring or slower wound healing than when silk is used. (2 tables, 4 figures, 7 references)

Thomas H. F. Chalkley.

Payrau, D., Pouliquen, Y. and Faure, J. P. **Heterografts of the cornea; experimental study and first clinical results (Part II).** Ann. d'ocul. **194**:123-132, Feb., 1961.

The first part of this study appeared in the January, 1961, issue of the Annales d'oculistique. Part I described the experimental work done by these authors and the present article describes their experiences with 36 human subjects in whom heterografts were done. In all cases dehydrated preserved grafts were used. In seven cases the cornea of a pig was used and all of these showed opacification and only one graft did not take. Fourteen heterografts were done using dog corneas. One of these again was extruded. Of the remaining group, seven of the grafts remained clear and were considered a therapeutic success. Most recently 14 heterografts were done using beef as a donor and in these cases results are too recent to be analyzed but appear to be not quite as good as those of the dog. The authors repeat that the antigen reaction appears to reside primarily in the cells of the cornea and largely in the epithelium.

An appendix gives the method for preparation of corneal extract of beef. (1 figure, 3 tables, 40 references)

David Shoch.

Sie-Boen-Lian and Li-Shao-Chen. **The possibility of a virus etiology of rodent corneal ulcer (Mooren).** Ophthalmologica **140**:311-322, Nov., 1960.

Two Cantonese patients with Mooren's ulcers demonstrated inclusion bodies in corneal epithelial cells. The article contains elaborate descriptions of these findings. Material from one of these ulcers was inoculated on rabbit and guinea-pig corneas, causing in each a nonspecific keratitis, which was not located marginally. From the guinea-pig cornea a virus was grown on a chick embryo yolk sac membrane. (10 figures, 8 references)

L. T. Post, Jr.

Tittarelli, R. and Zehetbauer, G. **The treatment of epidemic keratoconjunctivitis with local convalescent serum.** Ophthalmologica **140**:296-302, Nov., 1960.

Previous reports have suggested the effectiveness of systemically administered convalescent serum in the treatment of EKC. The authors have had the opportunity of treating 14 patients with con-

valescent serum instilled locally into the conjunctival sac. All the patients were treated during an epidemic which took place in St. Gallen, Switzerland, during the summer of 1958. As controls 21 patients were treated with local antibiotics alone. It appeared that the convalescent serum shortened the course and severity of the disease, tended to prevent the appearance of corneal lesions, and, used prophylactically in the fellow eye, protected it from involvement, or at least made the disease of far less moment. The simplicity of the treatment and the freedom from side effects is emphasized. The chief problem rests in obtaining convalescent serum of sufficient potency. The peak antibody titer is found at about one month from the onset of symptoms, but there is evidence to suggest that effective antibody titers persist for long periods of time. (1 table, 12 references)

L. T. Post, Jr.

Trantas, N. G. **Atrophy of the trabeculum corneo-sclerale.** Bull. et mem. Soc. franç. d'opht. 72:73-96, 1959.

The author reviews shortly the changes in the chamber angle as seen clinically in gonioscopy, their relation to glaucoma and the interpretations by various investigators; he also describes additional atrophic changes observed in this region by himself. He recognizes two special forms of atrophies, namely, localized grooves which could be located anywhere in the trabecular region from the ciliary band to the corneal side of Schwalbe's ring and extended trench formations especially over the posterior trabecular band; he also emphasizes the importance of what he calls the "red ring." This red ring should not be identified with Schlemm's canal, which appears as a delicate red filament. The red ring is the result of a reflux of blood, a hemorrhagic progressive blood imbibition of the trabeculum sclerocorneale. It is a sign that this struture was not destroyed. A retardation or lagging of this red band does not necessarily prove a definite destruction of the trabeculae but presents a disturbance between episcleral and intraocular pressure and the combined forces which regulate the outflow mechanism. All these signs and symptoms are not characteristic of chronic glaucoma only, but have been seen in various forms of uveitis, after trauma, and in one case of infantile glaucoma. These statements are documented by case histories. The skill in clinical investigation and the knowledge of the author concerning the analysis and interpretation of gonioscopic details were recognized during the discussion. (1 table)

Alice R. Deutsch.

Tsutsui, Jun, and Watanabe, Saeko. **Clinical evaluation of the precipitin test in the postoperative course of keratoplasty.** A.M.A. Arch. Ophth. 65:375-380, March, 1961.

Part of the donor cornea was used as the antigen in 14 cases and the hosts' immunological reaction was followed by means of precipitin tests on blood serum. Serum-antibody titer increased in eight cases between the fifth and twentieth postoperative day and reverted to negative between the tenth and fiftieth day. The authors feel that steroid medication is a significant aid in the prevention of opacities caused by donor-recipient reaction. (1 table, 21 references)

Edward U. Murphy.

8
UVEA, SYMPATHETIC DISEASE, AQUEOUS

Amalric, Barone, Besson and Lescure. **The relationship of congenital heterochromy to the syndrome of Claude Bernhard and the syndrome of Fuchs.** Bull. et mem. Soc. franç. d'opht. 72:97-111, 1959.

The diagnostic characteristics of congenital primary heterochromia were clari-

fied by reviewing a series of pertinent case histories. It was demonstrated that this anomaly frequently constituted a simple constitutional anomaly. On the other hand it was found to be associated with serious progressive ocular lesions or joined to a neuro-ocular syndrome. The potential dependency of primary simple heterochromia, sympathetic heterochromia, complicated heterochromia and their genetic inter-relationships were demonstrated on several genealogic tables. To this was added a report on correlative experiments on dogs.

Further studies of the interesting problem of heterochromia extended to related comparatively rare syndromes like the Wardenbourg-Klein syndrome, whose main features are heterochromia, deafmutism and displacement of the internal canthi. Another related syndrome is the syndrome of Georgiades which includes heterochromia, disturbances of the cervical spinal column, and the sporadic appearance of microphthalmos. (98 references) Alice R. Deutsch.

Brini, A. and Perte, A. **Studies on the ciliary body with the electron microscope.** Bull. et mem. Soc. franç. d'opht. **72**:56-72, 1959.

The ultra-structure of the pigmented and unpigmented epithelium of the ciliary body and of the zonula were investigated under the electron microscope and an effort was made to correlate morphologic findings with physiologic mechanisms. The eyes of swine and rabbits were the material of choice. It was possible to examine the rabbit eyes in vivo after injection of osmic acid and puncture of the anterior chamber. The endoplasmic reticulum, the changing phases of vacuole-formation, the aggregation of extra-cellular material and the transposition of the limiting membranes are discussed and demonstrated in a series of slides. The zonula was found to be in direct relation to the limiting membrane and apparently a derivative of this structure. The histochemical reactions showed a richness in tyrosine which is not characteristic of collagen structure but resembles the structure of fibrin, keratin, or myosin. The morphology in details of single zonula fibers also proved to be different from typical collagen fibers.

Jules François, one of the discussers, reconfirmed the authors' findings through his own research work with the electron microscope. Marwas, another discusser, insisted that he had reported similar findings fifty years ago, using only the light microscope. (12 figures, 13 references) Alice R. Deutsch.

Burian, H. M. and Allen, Lee. **Histologic study of the chamber angle of patients with Marfan's syndrome.** A.M.A. Arch. Ophth. **65**:323-333, March, 1961.

Specimens from three patients were studied in detail. The outstanding characteristics were a flat, long ciliary body with poorly developed circular and radial muscle fibers, prominent pectinate ligament fibers, and abnormalities in the trabecular meshwork and outflow channels. These findings are typical of lower vertebrates, in particular the dog in which the chamber angle is almost indistinguishable from that of a human being with Marfan's syndrome. (12 figures, 16 references) Edward U. Murphy.

Kimura, S. J. **Annual reviews. The uveal tract.** A.M.A. Arch. Ophth. **65**:457-467, March, 1961.

The literature from September 1, 1959, through August 30, 1960, is covered. (80 references) Edward U. Murphy.

Rocha, H. **Sympathetic ophthalmia. Does it occur without a perforating injury?** Bull. et mem. Soc. franç. d'opht. **72**: 113-127, 1959.

The various theories concerning the etiology of sympathetic ophthalmia are

reviewed, with emphasis on their theoretical and practical implications. Clinical, histological, and bacteriological examinations, audiological tests and hypersensitivity studies have proved that sympathetic ophthalmia is not a specific entity but could be placed with other groups of uveitis of unknown or known origin like meningo-uveitis, the Vogt-Koyanagi syndrome, and Harada's disease. The likeness and the diversities of these three symptom complexes are described with particular emphasis on their similarities. The discrepancies in the clinical picture which are noted when sympathetic ophthalmia is compared to Vogt-Koyanagi uveitis, are tentatively explained by a difference in the way of penetration of the causal agent, namely, direct penetration of the ocular coats is compared with distribution through other pathways.

The author includes the case history of a 28-year-old woman with a spontaneous bilateral uveitis. Clinically and histologically the diagnosis of sympathetic ophthalmia was established. Serial sections proved the absence of any perforation. (6 figures, 38 references) Alice R. Deutsch.

9

GLAUCOMA AND OCULAR TENSION

Armaly, M. F. and Rubin, M. L. Accommodation and applanation tonometry. A.M.A. Arch. Ophth. **65**:415-423, March, 1961.

This study shows that accommodation produces a significant reduction in ocular tension. When accommodation is completely relaxed, repeated applanation tonometry does not affect the ocular tension level. (7 figures, 5 tables, 4 references)

Edward U. Murphy.

van Beuningen, E. G. A. **Specification No. 5 for mechanical and electric Schiøtz tonometers and some remarks regarding the technique of calibration.** Klin. Monatsbl. f. Augenh. **138**:210-215, 1961.

The author states that Specification No. 5 of the American Committee for Standardization of Tonometers (October, 1959) has replaced Specification No. 4 of March, 1952. The new specification is given. Several suggestions for improvement of the calibration procedure are given. Gunter K. von Noorden.

Drance, S. M. and Carr, F. **A comparison of tonography with three Schiøtz weights in normal eyes.** A.M.A. Arch. Ophth. **65**:424-426, March, 1961.

From the data presented here, the coefficient of outflow in normal eyes was not markedly different when taken with different Schiøtz weights. This is in disagreement with the conclusions of a previous paper which appeared in 1956. The authors suggest three possible sources of error which were avoided in their study. (2 tables, 5 references)

Edward U. Murphy.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Thomas Viggers Murto, Trenton, New Jersey, died December 25, 1960, aged 69 years.

Dr. Samuel Henry Wilkins, Boston, Massachusetts, died February 2, 1961, aged 79 years.

ANNOUNCEMENTS

RETINA FOUNDATION

Clinical research fellowships of the Retina Foundation will be expanded upon completion of the Foundation's research building at the end of 1961. The training program includes concentrated work in general fundus diagnosis by indirect stereoscopic ophthalmoscopy and in retinal detachment surgery. Many opportunities and special training are available in various phases of clinical research. Details about one-year and two-year programs will be sent on request. Fellows not supported by other research or training grants receive adequate stipend.

Graduates of medical schools outside the United States and Canada must complete the requirements of the Educational Council for Foreign Medical Graduates to engage in clinical activities. Inquiries and applications should be addressed to Dr. Robert J. Brockhurst, 99 West Cedar Street, Boston 14, Massachusetts.

ROCHESTER COURSE

Beginning Monday, August 7, 1961, the Department of Ophthalmology of the University of Rochester, School of Medicine and Dentistry, will conduct a four-day graduate course of lectures and demonstrations in ophthalmology. An outstanding group of ophthalmologists of national prominence, augmented by several technical experts, will give a series of lectures and demonstrations of interest to all ophthalmic practitioners. Recent advances and observations in ophthalmology will be stressed.

The tuition fee for the course will be $60.00. This covers tuition and the banquet Monday night. Twenty dollars ($20.00) is payable with registration. The remainder of the fee will be payable on matriculation, Monday, August 7, 1961. Registration with check payable to order of University of Rochester, should be mailed to the Strong Memorial Hospital, Rochester 20, New York.

The Towne House Motor Inn, located near the University of Rochester Medical Center is the headquarters for the summer graduate course. Please address your request for room reservations to the Towne House Motor Inn, Mount Hope at Elmwood Avenue, attention Reservation Manager, who will make special arrangements for members of the course.

SOCIETIES

NASSAU ACADEMY

The inaugural meeting of the Section on Ophthalmology of the Nassau Academy of Medicine was held on Monday, May 22, 1961, at the Academy, with Wendell L. Hughes, M.D., chairman, presiding. John H. Dunnington, M.D., the guest speaker, presented a paper on "Complications of cataract extraction." Several interesting cases were presented by members of the section as part of the evening's program. The next meeting of the section will be on Monday, November 27, 1961.

TEXAS OFFICERS

New officers for the Texas Ophthalmological Association are: President, Jack B. Lee, San Antonio; vice president, James Scruggs, Waco; secretary, Harold E. Hunt, Paris. The next meeting will be in Austin on May 13 and 14, 1962.

TURKISH CONGRESS

The IV National Turkish Congress of Ophthalmology will be held at İzmir, Turkey, on September 13th to 15th. On September 16th and 17th, trips are planned to historical and tourist places in the neighborhood of İzmir (Perganon and Ephesus). Applications should be made to Prof. Selahattin Erbakan, Tip Fakültesi göz klinigi (devlet hastahanesi), İzmir, Turkey.

Officers of the congress are: President, Naci Bengisu; vice president, Süreyya Gördüren; secretary, Selahattin Erbakan; treasurer, Gülhan Slem.

MONTREAL SOCIETY

A special dinner meeting of the Montreal Ophthalmological Society was held at the Queen Elizabeth Hotel on May 31st, to honor Dr. Alfred J. Elliot on the occasion of his completion of 15 years as professor and head of the Department of Ophthalmology, University of Toronto.

Dr. Elliot is leaving Eastern Canada to take up a new appointment as head of the Ophthalmology Department, University of British Columbia, Vancouver. Dr. Elliot addressed the meeting on "Hypolacrimation."

Representatives from the Quebec Ophthalmological Society, Laval University, McGill University, Queen's University, University of Ottawa and University of Montreal read congratulatory messages. Dr. Elliot was elected an honorary member of the society.

URGENT REQUEST

The Uveitis Laboratory, University of California School of Medicine, San Francisco, is vitally interested in obtaining freshly enucleated eyes from patients with all types of uveitis and other endogenous inflammations. Attempts are being made to isolate etiologic agents from these eyes.

The eyes should be placed in a sterile bottle, packaged with the history and findings, and shipped as quickly as possible. Please send specimens special delivery, collect, and mark the package "Fresh Tissue Specimen—Rush." Do not freeze or use preservatives of any kind.

A report of isolations of organisms and pathologic findings, including a slide, will be sent to the contributor. Credit will be given in any resulting publications if desired.

Telegraph collect if specimen being sent.

Send eyes to

Samuel J. Kimura, M.D., Michael J. Hogan, M.D., or Phillips Thygeson, M.D.

University of California School of Medicine
San Francisco 22

Gift Order Form

Send to Ophthalmic Publishing Company, 664 N. Michigan Ave., Chicago 11, Illinois

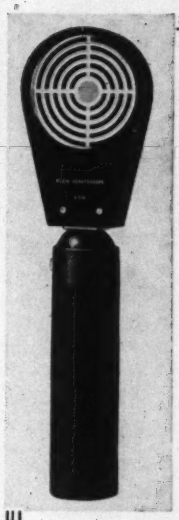
Please send the American Journal of Ophthalmology for one year to:

Name .....

Address .....

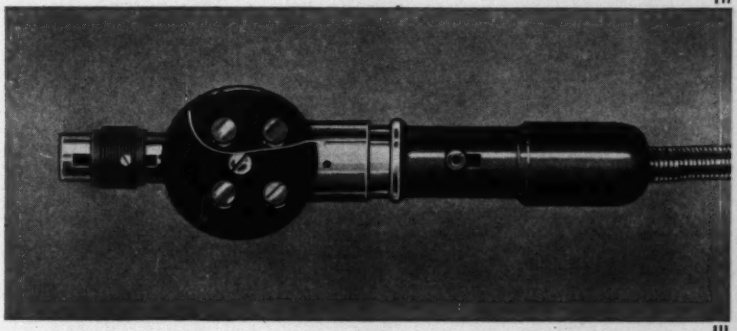
Sign gift card from .....

Your address .....



Diagnostic Accessories

The KLEIN KERATOSCOPE, illustrated alongside, provides a brilliant and clearly-defined reflected image of the cornea. It is invaluable for post-operative examination of corneal grafts; the ready detection of corneal scars and ulcers; for confirmation of corneal astigmatism and assessment of axis; and for demonstration of lenticular astigmatism, by showing that astigmatic eye has normal corneal configuration.



The KEELER 4-Dot FOCAL ILLUMINATOR shown above fulfills all the surgeon's requirements for external examination of the eye. By simple adjustment following examinations can be carried out: Focal illumination, hand slit-lamp examination: Fluorescein testing: Worth 4-dot near test: Scleral transillumination: Colour testing by white, red and green apertures.

FOR FULL DETAILS OF THE ABOVE, OR ANY OTHER ITEMS OF THE EXTENSIVE KEELER RANGE, PLEASE WRITE TO PHILADELPHIA ADDRESS GIVEN BELOW.

Keeler

KEELER OPTICAL PRODUCTS
INC.
5536 Baltimore Avenue, PHILADELPHIA 43, Pa.

When the growing
Things of summer
Bring grief to
Allergic eyes . . .

Prednefrin® 0.12%

OPHTHALMIC SUSPENSION

. . . provides prompt control of the ocular symptoms of summer allergies throughout the entire season. PREDNEFRIN offers these therapeutic advantages:

- Checks inflammation and itching.
- Soothes and lubricates — within minutes reduces redness, improves the eye's appearance and "feel."
- The Allergan microfine suspension provides a long-acting, repository-like dosage form.
- The non-polar form of the steroid for efficient penetration and absorption.

Formula:

PREDNEFRIN 0.12% contains:
Prednisolone acetate..0.12%
Phenylephrine HCl....0.12%
Methylcellulose 0.12%

Dosage:

1-2 drops in conjunctival sac, two to four times a day.

Supply:

In 5 cc. and 10 cc. plastic dropper bottles — Rx only.

ALLERGAN
PHARMACEUTICALS
Los Angeles 17, California